The New England
Journal of Medicine

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Volume 231 OCTOBER 5, 1944 Number 14

THE APPLICATION OF PULMONARY PHYSIOLOGY TO THERAPEUTIC PROCEDURES*

With Special Reference to the Use of Oxygen

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BOSTON

DURING many years of experimental work in what I call mammalian or medical physiology, I have been drawn again and again to observations on the lungs and, on looking back, am struck by the diverse lines of inquiry that have been necessary. Physiology, anatomy, pathology, surgery, all have had their place, with emphasis on the fact that neither the experimenter in the laboratory nor the agent of disease can succeed in doing just one thing to the lungs. The functions, structure and functional relations of lung tissue are so vital, so delicately ordered and so immediately of consequence to other parts of the body as to make it necessary to view events in them through a number of fundamental medical disciplines.

Reduced to simplest terms, breathing originates in the respiratory center in the medulla. The metabolism of this collection of nervous tissues continuously produces carbon dioxide. When carbon dioxide reaches a certain concentration in this center, a series of impulses are discharged that result in inspiration. Since carbon dioxide is a substance that diffuses rapidly through a watery medium, it is to be expected that as it accumulates in the center it will also be diffusing out toward the blood. If one breathes a gas mixture containing 5 to 10 per cent carbon dioxide, the blood going through the respiratory center will contain more than the usual amount of the gas and outward diffusion will be slowed, which, in turn, will favor the more rapid attainment of discharge concentrations and a consequent increase in breathing.

One may believe that the discharge concentration for the center is not always the same. It depends on the setting or condition of the center at the moment, somewhat as one might expect to have to apply a hotter poker to a pile of damp powder to explode it than would be necessary for dry powder. It is this setting of the center that is most important. There are few drugs that stimulate breathing, but there are many that depress it. Ether, alcohol and chloroform all depress breathing when they pass beyond their initial effects. Morphine is notable in this direction, and the barbiturates all produce a certain degree of anoxia in animals breathing air if they are given to the point of producing anesthesia. Far more important than any drug for its dampening effect on the respiratory center is lack of oxygen. By this is meant that essential automatic discharge of impulses by the center as a result of the accumulation of carbon dioxide is progressively hindered as anoxia develops. The increase in breathing following inhalation of 7 per cent carbon dioxide becomes less if it is repeatedly tested during anoxia produced slowly by means of carbon monoxide. It is quite true that in the carotid and aortic bodies chemoreceptors are present that are stimulated by oxygen lack, but the hyperpnea resulting from oxygen lack is a weak affair compared with what is obtained from carbon dioxide in the presence of normally ample oxygen. Furthermore, stimulation of breathing through oxygen lack is in many reactions similar to nerve stimulation. To be effective there must be a sudden rise in the intensity of the stimulus. Anoxia, as one usually sees it, develops insidiously and may become quite marked without noticeably disturbing the rate or volume of the breathing. In summary, so far as anoxia is concerned, the reactions of the central nervous system are not on the whole very serviceable against the progress of the condition. It is curious that evolution has not resulted in better protection by the central nervous system against oxygen lack, but the fact is that anoxia begets anoxia, an axiom too often forgotten in the management of patients.

If oxygen lack is accompanied by a gradual loss of efficiency in the central mechanism controlling breathing and thus by depreciation of the oxygen

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A lecture delivered at the Children's Hospital, Boston, on March 30, 1944.

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intake, its results on the smallest blood vessels are even more significant. It was Krogh's idea that anoxia is responsible for many localized dilatations of capillaries. Lewis, a little later, concluded that as a result of anoxia, and of trauma of the most varied sorts, an "H substance" is formed locally and causes the reaction in question. This

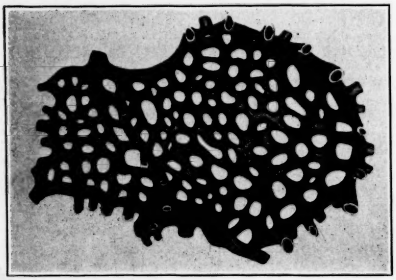

FIGURE 1. *Reconstruction of Capillaries in the Walls of Alveoli (x280) (reproduced from Miller[1] by permission of the publisher).*

Note the absence of long capillaries. The total surface area for gas diffusion provided by this close net is estimated at 140 square meters in a normal adult.

idea, supported by a variety of ingenious experiments, induced many people to neglect Krogh's position. He considered lack of oxygen to be a special form of chemical injury, which caused capillary dilatation through formation of a variety of substances, not of a single histaminelike product. This conception is probably more nearly correct than the simpler one of Lewis and puts anoxia in the special position it deserves. I know of no exception to the fact that systemic capillaries in all parts of the body dilate as a result of oxygen lack. Some are less responsive than others, but the rule seems to be that when a tissue becomes anoxic the capillary bed becomes larger. In many cases dilatation is accompanied by increased permeability, so that edema also occurs, but in the experience of most investigators abnormal leakage is not an essential companion of larger capillary diameter unless the change is extreme.

Our concern today is with the lung capillaries. In spite of evidence purporting to show it, there is no reason to believe that these capillaries possess active powers of contraction and dilatation as is the case with practically all the systemic vessels. This does not mean that their diameter does not change, nor that at times there are capillaries that are not conducting blood and that may later be filled by a moving current. These changes are, I believe, passive and depend on variations in the output of the right ventricle or a rise in pressure in the pulmonary veins. The capillary net in the lungs is for the purpose of gathering oxygen to serve the entire body and for eliminating all the carbon dioxide produced. The vessels lie in a tissue so delicate that it is structurally almost the foam the ancients believed it to be, and is at the same time highly elastic. The lungs must meet the needs of the body when the cardiac output is 4000 cc. a minute and when it rises abruptly even to 30,000 cc., and this result is best obtained if the vascular bed is large enough for the greatest needs, and so arranged as to give all parts of it a practically equal chance to receive increased amounts of blood instantly and without any adaptive opening reaction (Fig. 1).

That the lung capillaries do not dilate adaptively as a result of oxygen lack does not exclude them from the second effect of anoxia, — namely, increased permeability, — and anoxia does make these vessels leak abnormally, a fact all too apparent as one watches the slow progress of pulmonary edema or, perhaps even more frequently, as one looks at the lungs at autopsy.

It is necessary to appreciate certain anatomic and physiologic facts and deductions about the lung capillaries. The situation to be examined is provided by a diagram (Fig. 2) constructed

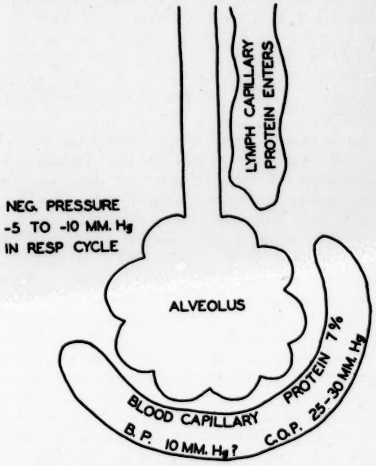

FIGURE 2. *Diagram of Certain Fundamental Conditions That Must Be Considered in Connection with the Formation and Removal of Pulmonary Transudates and Exudates.*

for the lungs on the basis of what is known to be operative in the case of systemic capillaries. In this diagram there is a capillary containing blood with a normal plasma protein content of 7 per cent, and this protein exerts an osmotic pressure — the colloid osmotic pressure of the

plasma of 25 to 30 mm. of mercury. In most systemic capillaries this force, which attracts water into the vessels, is opposed by the capillary blood pressure derived from the left ventricle and of about the same magnitude. There is thus a balance of forces that controls movements of water and dissolved salts through the capillary endothelium. In the lungs the colloid osmotic pressure drawing in water is necessarily 25 to 30 mm., but the opposing capillary blood pressure is not known. It must be low, and 10 mm. is a fair value. This means that in the lungs relative dryness of the tissue is substantially safeguarded and that under normal conditions extravascular fluid is in reality intracellular fluid. There are, however, local disturbers of this balance. The walls of the lung capillaries are separated from the alveolar air by a single layer of extremely thin epithelial cells. At each normal inspiration the pressure in the trachea becomes negative (−3 mm.), and this effect extends through the bronchi into the alveoli. At the end of inspiration, air having entered the alveoli as a result of atmospheric pressure, the intra-alveolar pressure becomes zero and rises slightly during expiration. This means that for outward filtration of water during inspiration an element of suction is added, and thus the filtering pressure is above 10 mm., and since a negative intrapulmonic pressure of 50 mm. may readily result from the obstruction of the trachea, it is clear that high filtering-out pressures may accompany half the respiratory cycle over long periods of time. It is true that the expiratory phase of breathing reverses the state of affairs, and that with the lung tissue wholly normal mechanical conditions that would result in the production of significant capillary leakage do not occur. But one must bear in mind that there is a single restraining influence for keeping water in the lung capillaries, which is fixed in the sense of being unalterable by local changes — the concentration of the blood proteins and their colloid osmotic pressure.

The other factors in the diagram are changed more or less readily, and all more readily in the direction of production of edema than against it. Thus, the permeability of the capillary endothelium may be increased by anoxia and by the action of drugs. The pressure in the lung capillaries is hard to disturb because of the immense area of the vascular net and the readiness with which expansion can be induced, but increases in pulmonary capillary pressure accompany cardiac disease, particularly while the right ventricle is still competent and a high-pressure head for outward filtration of fluid is maintained. This pressure may be enhanced by increased negative pressure in the alveoli during dyspnea. The human system depends for lung dryness on what Meltzer[2] years ago termed "a factor of safety" inherent in the predominance of osmotic retention of capillary water. This "safety" is assailable from a number of directions, and the attack is never achieved by a single one of the assailing forces but practically always by many of them. Of the factors leading to edema, increased permeability of the lung capillaries is by far the most important and of all the possibilities for inducing it, anoxia is infinitely the most frequent.

There are two other items in the diagram that have not been mentioned. The first of these is the negative intrapleural pressure. Graham[3] in 1921 expressed the belief that prolonged increase in the negative intrapleural pressure may suck fluid through the pleura and cause pleural effusion. This is true. Indeed, it has been shown that apparently normal men subjected to hard physical exercise accumulate pleural transudates. It is apparently the increased breathing of the exercise that does this, through the sucking action of lowered intrapleural pressure during vigorous inspiration.

The final component of the diagram is a lymphatic. Wherever lymphatics are found in the body their principal function is the carrying off of small amounts of protein that have left the blood capillaries. In addition to this regular function, the lymphatics take away other things in the tissues not readily absorbed by the blood vessels, among these being bacteria, foreign particles of many varieties and the detritus accompanying inflammation. The distribution of lymphatics is most profuse in parts of the body that are essentially surfaces between the interior of the body and the outside world. A well-known example is the extraordinary number and size of the lymph capillaries in the nasopharyngeal mucosa and in the mucosa of the female genital tract. In these regions, in addition to the constant possibility of infection, with the necessity of removing highly proteinized exudates, there are rhythmic periods of edema due to transudation of fluid containing much protein. The lungs seem to be free from any need to be constantly cleared of excess tissue fluid, but it is a fact that they are as profusely supplied with lymphatics as is practically any tissue in the body. Lymphatics are constantly seen in lung sections, but one has a poor idea of their number or extent and of their ability to rid the lungs of fluid. Over the surfaces of the arteries, veins and bronchi are lymph vessels, obviously large vessels. Their ends do not reach into the actual alveolar walls but stop as blind terminals in the walls of the alveolar ducts. An idea of the extent and capacity of the lung lymphatics is gained by a reconstruction of a typical plexus about a pulmonary vein (Fig. 3).

In spite of this profusion of lymph channels, it is puzzling to find that the arrangement for delivering their contents into the blood is curiously inadequate. The fact is that all the lymph from the lungs except a very small amount from the upper part of the left lung empties into the right sub-

clavian vein by way of the right lymphatic duct, which is usually a short tube not more than a millimeter in inside diameter. This vessel is an astonishingly small bottleneck at the delivery end of a large reservoir for accumulating proteinized and waste-containing fluid.

Let us now consider the bearing of these and other matters on asphyxia of the lung capillaries.

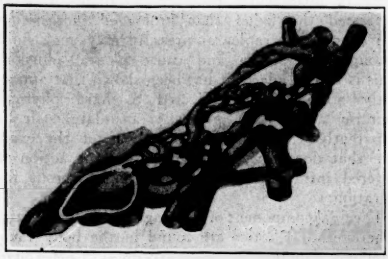

FIGURE 3. *Plexus of Lymphatics about a Pulmonary Vein (x15) (reproduced from Miller[1] by permission of the publisher). This particular vein was situated in an interlobular septum.*

Their endothelium is in the peculiar situation of receiving oxygen directly from the air, not at second hand from the blood. From the latter, all that the endothelium can gain is the precarious supply still remaining in the venous blood. This makes the lung capillaries dependent on the oxygen content of the alveoli in whose walls they lie. The body in general gets oxygen through the entire absorbing surface of the lungs, but the situation of the alveolar capillaries is not so safeguarded, and as transudation from these vessels begins they are steadily more and more widely separated from their oxygen supply.

To illustrate, there is employed a section of lung where exudate is forming and has formed (Fig. 4). One should observe the clear space under the pulmonary epithelium, which has been pushed loose in a continuous sheet. There is exudate in the alveolus, which may interfere with ventilation, and a layer of fluid under the epithelium and between it and the capillary wall. There are three possible ways of getting rid of this exudate. It may drift up through the air passages and be coughed out, may be broken down by enzymes and absorbed into the blood, or may drain off through the lymphatics. This last pathway is immediately available for interstitial exudate, which, as it accumulates in the alveolar wall, must eventually surround a capillary lymphatic terminal and enter it, to move slowly toward the right lymphatic duct through the enormous lymphatic network described, in every case traversing at least one lymph node. It is not surprising that when one causes continuous and copious leakage of lung capillaries, one finds bronchi and blood vessels surrounded by rings of fluid. In such a case, as is illustrated in a low-power photomicrograph (Fig. 5), most of the thin-walled intercommunicating lymphatics have apparently been ruptured, and lymph drifts along the blood vessel as a grossly visible sleeve of dilute blood plasma, which may or may not reach the narrow neck of the funnel — the right lymphatic duct.

All this indicates clearly enough that the lungs are not provided with any too adequate means of getting clear of exudates once they are present, and obviously exudates interfere profoundly with the entrance of air into alveoli and the passage of oxygen into lung capillaries. So in the lungs as well as in the respiratory center anoxia begets anoxia.

How vulnerable the lungs are to oxygen lack can be approximately shown by an example. If the lungs of a normal dog are ventilated artificially so that the mechanical factors in breathing are held constant and lymph is collected from the right lymphatic duct, the flow of lymph increases and the lymph becomes bloody when the oxygen in the air is reduced to 8.5 per cent; if one shifts back to 100 per cent oxygen, the flow soon falls to normal and the red cells disappear.[4] It must be realized that this experiment has to be a rather crude one, carried out on a curarized animal under constant conditions of artificial respiration, which inflates the lungs through positive pressure and allows expiration to occur passively. Positive-pressure ventilation does not reach the alveoli

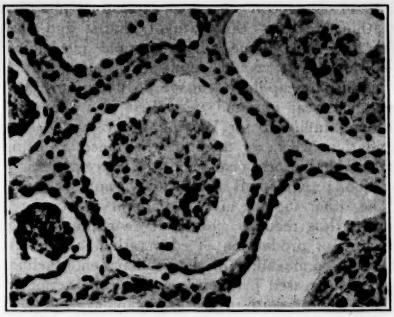

FIGURE 4. *Section of an Exudate-Containing Lung (x345) (reproduced from Miller[1] by permission of the publisher). The epithelium lining the alveolus in the center of the figure has been pushed off as a continuous sheet. Certain of the cells are more swollen than others. The alveolus in the upper right of the figure shows clearly the epithelium before and after an exudate has raised it from the surface of the alveolar wall.*

throughout the lungs with anything like the efficiency of the negative-pressure ventilation of normal breathing. It is thus quite probable that the transudation reflected in the lymph comes from parts of the lung that are receiving little or none

of the oxygen-poor mixture employed, and that the capillary endothelium of the lungs is much more resistant to oxygen lack than the experiment indicates. But even if this is the case, it is obvious that parts of the lungs have been affected and that a return to adequate oxygen in the air is followed by prompt restoration to normal. If, however, the experiment is carried out more slowly and abnormal capillary leakage is continued for some time, restoration of normal conditions through the use of oxygen is greatly delayed or does not occur during the experiment. Furthermore, if the pressure in the lung capillaries is increased by tightening a clamp on the pulmonary veins when oxygen-poor air is used for ventilation, the lung lymph changes in a very short time into what is practically blood.

FIGURE 5. *Section of the Lung of a Dog with Severe Exudation (x18).*
Note the rings of relatively clear fluid surrounding the blood vessels and bronchi.

One may be deceived in regard to the onset of lung edema by the fact that the lungs are so much larger than the resting subject requires. If the process begins in a dependent part of a lobe and transudate travels up bronchi and obstructs neighboring bronchi, no attention is paid to it until the patient, at rest and so requiring the least possible oxygen, takes a distinct turn for the worse. When this happens, the lungs, as receiving structures, where gas exchange can occur readily, are greatly reduced in functional size and the safety inherent in their normal oversize is lost. The probability is that the condition will progress further, not only by local spread of excess fluid in the lungs but also because as anoxia increases the efficiency of the respiratory efforts often becomes less.

It is my task to speak of but one of the measures for combating anoxia. It is the obvious one — administration of oxygen. The therapeutic use of oxygen in 1914, when I entered the Peter Bent Brigham Hospital as a house officer, was negligible, but this entire lack of reliance on oxygen has given way to a better appreciation of what it can accomplish. The reasons why there is still too little use of oxygen are as follows. In the first place, anoxia is essentially progressive. If the physician begins to use oxygen when he is sure that it is needed, he has incurred a handicap that is usually insurmountable. The time to begin to use oxygen is before there is any certainty it is needed. Secondly, the present methods for administering oxygen are expensive and inefficient. It will probably be a long time before oxygen therapy is inexpensive, but that is not of so much moment as is inefficiency. Pure oxygen has five times the power to penetrate exudates and reach anoxic parts of the lungs and the blood going through them that air oxygen has. Pure oxygen breathed continuously for eight to twelve hours is of itself irritating, to the respiratory passages, but minor interruptions from time to time are enough to dispose of this danger, which is not a potent one unless oxygen is breathed under a pressure of two to three atmospheres. Oxygen tents often do much for patients, but they are leaky, inefficient affairs in which the oxygen concentration is usually well below 60 per cent. Mask administration of oxygen has improved, and if the experience gained during the war is utilized it can be carried much farther. Lastly, there is a failure to realize the possible advantages to be gained even from poorly administered oxygen in many ordinary conditions. For example, there is no drug that gives such great subjective relief or such valuable rest in dyspnea as does morphine, but this drug dampens

the respiratory center and thus promotes anoxia. There is no reason why the use of oxygen with morphine should not allow all possible benefit from the sedative without the progression of anoxia. Similarly, after operations, particularly in elderly patients with fairly rigid chests and pain on breathing that still further restricts respiratory movement, oxygen therapy may for a time permit the economy of lung movement that the patient involuntarily provides, and the use of a much needed sedative may be robbed of some of its danger.

It would be possible to multiply such illustrations indefinitely. These are enough, and they, with all that has been said above, may help to enforce further the two principles that the laboratory has learned are the master words in oxygen therapy: anoxia begets anoxia, and if real benefit is to be expected from oxygen, it should be used before the need is certain.

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TROPICAL DISEASES OF THE SKIN*

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IN THIS paper will be discussed five diseases in which cutaneous manifestations constitute either the whole clinical picture or an important part of it. Three of these diseases, yaws, pinta and verruga peruana, are almost entirely confined to the tropics, and the other two, cutaneous leishmaniasis and leprosy, are at least more prevalent in tropical than in temperate climates.

The present interest in tropical diseases is mainly due to the possibility of their being contracted by the members of our armed forces. Of the diseases in question, the likeliest ones to affect our soldiers and sailors are cutaneous leishmaniasis and leprosy. It is almost certain that a few men at least will contract these diseases, although in the case of leprosy there may be no active manifestations for a number of years after their return to the United States. Information about tropical diseases of the skin will also be of value to medical officers whose duty it may be to take care of native populations, both during and perhaps for some time after the war.

Yaws

Yaws (frambesia tropica) is an infectious disease caused by *Treponema pertenue*, an organism that is morphologically identical with *T. pallidum*. The disease occurs almost exclusively in dark-skinned races, especially Negroes. The fact that the white man rarely suffers from yaws is probably due to personal hygiene and not to any racial immunity. The geographic distribution of yaws is widespread and includes parts of equatorial Africa, many islands of the Pacific, Burma, Thailand, some islands of the West Indies and tropical parts of South America. The disease is contracted most often in childhood, usually by personal contact, although in some cases the infection is transmitted directly by certain flies. The initial lesion or so-called "mother yaw" may not be observed. It does not remotely resemble the chancre of syphilis, and is merely the largest lesion of the type of the ordinary secondary or frambesiform eruption.

The typical eruption of yaws — frambesiform — begins as small papules that tend to coalesce, soften and discharge a fluid that forms typical amber-colored crusts. It does not resemble any ordinary eruption of syphilis but rather suggests an impetigo. The eruption lasts for months up to a year or two and disappears spontaneously without leaving any permanent trace. Another characteristic eruption is a hyperkeratosis of the soles, called "crab yaws" by the natives of the West Indies. The term is used because the affected persons walk like a crab, owing to soreness caused by secondary infection. The eruption is not due merely to walking barefoot, since barefooted natives who suffer from syphilis do not often present this characteristic eruption.

There are two frequent manifestations of early syphilis that have never been observed in yaws. They are iritis — or iridocyclitis — and alopecia, including both a diffuse thinning of the hair and the patchy so-called "moth-eaten" type so characteristic of syphilis.

There are four features that yaws and syphilis have in common. In both diseases the causative organisms are morphologically identical, both of them give the same serologic reactions, both yield to arsphenamine and allied drugs and to bismuth, and in both the late destructive tertiary lesions are clinically indistinguishable. There are, however,

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

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many points of dissimilarity between the two diseases, which are sufficient to prove that they are separate though allied infections.

One of the striking differences between yaws and syphilis is that in yaws the infection is usually, if not always, extragenital. Again, in the secondary period there are no lesions of the mucous membranes, the absence of vaginal mucous patches probably accounting for the failure of infection by sexual intercourse. Another difference is the absence of intrauterine infection in yaws, there being no lesions in children that suggest congenital syphilis.

Yaws is a milder infection than syphilis because it does not affect to any appreciable extent the vital structure of the body. It is doubtful whether the viscera are affected by yaws, and lesions of the cardiovascular and central nervous systems are mild compared with those of syphilis. The statement is often made that no one seems to die of yaws, although in the late stages severe deformities may result from lesions of the skin, mucous membranes, bones, tendons and joints. The lessened tendency for yaws to attack the blood vessels is seen in histologic sections of cutaneous lesions. These do not show the same tendency as the lesions of syphilis to produce endarteritis. Yaws also yields to treatment more rapidly than does syphilis.

There are differences between the immune reactions of yaws and of syphilis, but eventually, at times after ten years, there is a complete cross immunity between the two diseases. This is well shown in the island of Guam, where most of the natives are immune to syphilis, since they have been infected as children with yaws.

Pinta

Pinta, like many other tropical diseases, has numerous local names. In Mexico, for example, it is called *mal del pinto*, in Colombia *carate* and in Venezuela *cute*. Pinta is an infectious disease mostly confined to the American tropics. It is caused by a treponema that is morphologically identical with the organism causing syphilis and yaws.

For many years the disease was thought to be due to a fungus, this theory persisting for eleven years after it was first shown that the serologic tests were positive in a large proportion of cases. By 1930, it was shown that the serologic reaction with both complement-fixation and flocculation tests in the pigmentary stage was almost 100 per cent positive. This was comparable to the serologic changes in syphilis and yaws. After the discovery of the causative treponema in 1937 by Armenteros and Grau Triana, the fungus theory was discarded.

The greatest incidence of pinta is found in Colombia and the southern half of the Republic of Mexico. A careful survey made a few years ago in Mexico disclosed the presence of over 270,000 cases. The disease affects chiefly the dark-skinned races, including Indians, Negroes and those of mixed blood. It is rarely seen in Whites. This fact helps to substantiate the claim that the disease is caused by personal contact and not by the bite of an insect or other arthropod. At least there is no definite knowledge concerning a possible insect vector.

Soon after the discovery of the causative organism, Leon y Blanco went to Mexico and proved that the disease is inoculable in man and that syphilis gives no immunity to it. The same investigator showed that a primary scaly plaque represents the initial lesion, which is often followed by nondescript secondary lesions of the skin. Eventually, the pigmentary stage ensues and lasts for years or decades. Previous to the discovery of a possible primary and secondary stage, the pigmentary disturbances were thought to constitute the entire picture of pinta.

The pigmentary stage consists essentially of slaty-blue patches appearing especially on uncovered parts as freckles or diffuse areas. Eventually a partial depigmentation appears, and if untreated the process in some cases continues until the patches are completely devoid of pigment. The eruption is then indistinguishable from ordinary vitiligo and is a permanent defect, the normal pigment never returning.

The serologic reaction in pinta is positive in nearly 100 per cent of cases in only the late (pigmentary) stage, whereas in the primary stage it is negative and in the secondary stage, when recognized, is said to be positive in 60 per cent of cases. In this regard pinta differs from the other two treponematoses, syphilis and yaws, in which the strongest positive reactions occur in the secondary stage and gradually lessen in the late stages. As a rule, there are no abnormalities in the spinal fluid in pinta.

The typical slate-blue color is due to the large number of melanophores in the cutis and not, as was originally thought, to the action of fungi.

Pinta, in the vast majority of cases, is an essentially harmless disease, except for the cosmetic deformity, which in some cases is severe. Those who suffer from pinta are apparently able to work as hard as are others who are not affected with the disease.

Cutaneous Leishmaniasis

Cutaneous leishmaniasis may be divided into the type seen in parts of the Old World and known as Oriental sore, Aleppo boil, Biskra button and so forth and the type appearing in the Western Hemisphere, known as American or mucocutaneous leishmaniasis. Both these types are caused by parasites, called "leishmaniae" in honor of Colonel Sir William Leishman, who first discovered them in kala-azar. The parasites causing the two types are morphologically indistinguishable in microscopic preparations made from scrapings and in cultures.

Oriental sore has a widespread geographic location, including Africa, Asia and parts of Europe. In Africa it occurs along the Mediterranean coast. In Asia Minor it is especially rife in Syria, Palestine and Armenia. It is endemic in the southern and eastern parts of Asia, and in Europe it occurs in Greece, Italy, Sicily, Cypress and Crete. This incomplete list shows numerous areas in which our armed forces are exposed to this disease.

Oriental sore may be contracted either by the bite of some species of sandfly (Phlebotomus) or by personal contact, as from one child to another. The disease is also occasionally transmitted by the common housefly. In certain areas dogs are infected, especially about the snout, and constitute a reservoir for the parasites.

The incubation period of Oriental sore varies from a few weeks to many months or at times a year. The eruption begins as small papules that enlarge and form a buttonlike plaque several centimeters in diameter. Eventually it becomes an ulcer covered with adherent crusts. It does not suggest the appearance of a boil, and the term "Aleppo boil" is therefore a misnomer. Healing is usually followed by scars, which may be disfiguring. There may be a single lesion or several, as many as a hundred or more having been observed.

Oriental sore is usually confined to the skin and as a rule occurs on the uncovered parts of the body. In the vast majority of cases it heals within a year as the Turkish name *habel-seneh* ("button of one year") indicates. In rare cases the disease lasts for many years. As a rule, when the eruption clears spontaneously or from treatment it is followed by permanent immunity. In extremely rare cases there is a recurrence. The disease is purely a local one and causes no constitutional symptoms.

The eruption must at times be differentiated from that of syphilis, tuberculosis, blastomycosis, ecthyma, bromoderma and tropical and other ulcers. An unquestioned diagnosis depends on finding the parasites in smear preparations — stained by Wright's method — or in cultures. In difficult cases, help has been given by intracutaneous tests of material from killed parasites.

Innumerable methods of treatment have been tried, with varying success. Excellent results have been obtained with x-rays and grenz rays, which, however, are not generally available. Care must be used with escharotics, since the disease is not a serious one and constitutes only a cosmetic defect. Excellent results have been claimed by freezing with solid carbon dioxide. Prophylactic treatment includes personal hygiene and the use of insect repellents. Sleeping under nets with forty-five holes to the square inch is also recommended.

The *American type of cutaneous leishmaniasis* is limited to the Western Hemisphere. It has been seen in every country of South America except Chile, in Central America and in the Yucatan Peninsula. The disease in the majority of cases is an occupational one, and is seen most often among foresters in Brazil, workers on tea plantations in Paraguay and chicle pickers in Guatemala and Yucatan. It is probably caused as a rule by the bite of some species of Phlebotomus, although infection by personal contact is possible. The causative organism is identical in appearance with that of the other types of leishmaniasis.

The American type differs from Oriental sore in its tendency to last for years and to attack the mucous membranes of the nose and throat, as it does in 15 to 20 per cent of cases.

The cutaneous lesions consist of one or more ulcers, occasionally a hundred or more. At first glance they appear to be nondescript, but they usually have a halo that is red and edematous. Lesions of the nose and throat, if present, usually follow cutaneous lesions by years and may be extremely deforming.

Treatment of cutaneous lesions by tartar emetic gives satisfactory results, but this remedy is not so efficient for lesions of the mucous membranes.

Verruga Peruana

Verruga peruana (bartonellosis) is now known to be one phase — the other being Oroya fever — of a disease that has probably existed in Peru for centuries. It has recently been observed in both Colombia and Ecuador.

Little was known of verruga peruana until 1870, when a railroad was built over the Andes. A violent epidemic resulted in which 7000 laborers died and 100 American and British engineers contracted the disease, half of them dying of it. In 1885, a brilliant young Peruvian medical student allowed himself to be inoculated with the harmless verruga peruana and died of severe Oroya fever. This convinced the Peruvian physicians that the two types probably represented the same disease. In 1913, Strong and others forming a commission from Harvard University visited Peru and concluded erroneously that verruga peruana and Oroya fever were separate diseases. In 1909, the causative organism, which is now thought to be a rickettsia, was discovered by Barton and was successfully cultured in 1926 by Noguchi and Battistini. Monkeys were inoculated by Noguchi with a culture from a case of Oroya fever and verruga peruana resulted. A year later, Mayer and Kikuth in Hamburg inoculated monkeys from a case of verruga and produced fatal Oroya fever. There was also a physician in Lima who accidentally inoculated his finger while giving a transfusion to a patient dying of Oroya fever. Fortunately he developed verruga peruana of the harmless type and recovered. From these facts it seems clear that verruga peruana and Oroya fever are different phases of the same disease.

Oroya fever is a most serious disease, with an average mortality of about 40 per cent, and presents the symptoms of pernicious anemia, with a sudden and tremendous drop in the red-cell count. Verruga peruana, after the stage of incubation, is also accompanied by febrile symptoms and anemia, but the latter is of the simple type. After a period of several months, an eruption appears and the patient is then on the road to recovery. The eruption is a unique one and consists of lesions that resemble pyogenic granulomas, senile angiomas or a general sarcomatosis. The eruption disappears spontaneously in a few months, and the patient is thereafter immune.

The causative organism is seen in the red cells of the peripheral blood in varying numbers (from one to ten or more). In culture it appears as rod-like bodies or as cocci.

The vector was proved to be night-flying species of Phlebotomus, whose habitat corresponds exactly to the areas where the disease is contracted. This is in deep ravines at an altitude between 2800 and 9000 feet. Most of the inhabitants of these ravines contract the disease in infancy or early childhood, when it causes only mild symptoms. There is no known specific treatment. Prophylaxis is all important. Townsend states that no one ever contracts the disease in Peru unless he has spent one or more nights in the infected ravines.

Leprosy

Leprosy is a serious disease that carries an undeserved stigma. This is partly due to the Biblical descriptions of a disease that was in all probability the same as the one now called leprosy. The disease has a world-wide distribution; although it exists in cold and temperate climates, its greatest incidence is in the tropics. It has been roughly estimated that there are 3,000,000 lepers in the world, about 30,000 of whom are in the Western Hemisphere. In the United States, it is estimated that there are 1000 or more cases, and in New York City there are always 25 or more cases known to the health authorities. All the latter are imported cases.

Contrary to popular belief, leprosy is not highly contagious. To contract the disease it is usually necessary to be exposed to it for long periods, especially in hot and humid regions. The method of transmission is not known, although infection of the nasal mucosa by the fingers is thought in many cases to be the cause. The disease is apparently not contracted by sexual intercourse.

Leprosy affects all races and both sexes and is oftenest contracted in the fifth to the twentieth year of life. The disease is neither congenital nor hereditary. It is undoubtedly caused by *Mycobacterium leprae* (Hansen's bacillus), even though the postulates of Koch have not been fulfilled. The disease is strictly confined to man and does not affect any of the lower animals.

The terminology of leprous lesions has been the source of considerable confusion. At the present time, one speaks of the two essentially different types as lepromatous, — formerly called nodular, — and neural, which can be subdivided into pure neural, maculoanesthetic and tuberculoid. The neural type has the signs and symptoms of a peripheral neuritis, the disease not affecting the brain or spinal cord. The neural type is the one oftener seen in the tropics and is decidedly more favorable in prognosis than the lepromatous type. It may cause severe mutilations, but the disease may become arrested and the patient live for decades thereafter.

One of the numerous problems to be settled in the future is why the disease is transmissible in some regions and not in others. For instance, Louisiana, Texas and Florida are now practically the only endemic centers in the United States. On the other hand, although there are always lepers in New York City, there is no case on record in which a person has contracted the disease in or near this city. In every case the person has spent more or less time in a part of the world where the disease is endemic. It therefore seems eminently proper to allow lepers in New York City to go at large, although they must report at intervals to the local health authorities.

The only way to eradicate leprosy is by segregation. In my opinion, there is as yet no specific remedy for the disease.

140 East 54th Street

THE GOAL OF AN EYE-HYGIENE PROGRAM FOR SCHOOL CHILDREN*

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BOSTON

THE title of this paper implies that there should be some sort of program directed toward the maintenance of eye health in all schools. Such a program need not be expensive, requiring equipment, personnel and time, nor so extensive as to include a complete eye examination by a competent ophthalmologist, let us say three or four times during the child's school life. Its object is best expressed as a consciousness on the part of school administrators, teachers and pupils alike of the value of normal, comfortable vision to progress in health and education, coupled with a desire for positive action. It can take such form as facilities available in the locality permit and the support of the local school authorities provide. The program may range from tried and true yet simple procedures, such as annual medical inspection and tests of visual acuity for distance (the Snellen test), to the complete and periodic examination of each child by a competent ophthalmologist. It may be extended to include psychophysiologic studies of certain groups of children such as those presenting symptoms of reading disability — formerly referred to as congenital word blindness. It may include provision for instruction concerning the care of the eyes (personal hygiene) and accident prevention, and may stress the importance of paying more attention to the eyes during the routine medical inspection. It may furnish special educational facilities for the visually handicapped child. It may provide for better school buildings, artificial illumination, desks, printing of schoolbooks, as well as other printed and mimeographed material, window shades and wall paint. It may provide for good blackboards, properly located and cared for, to ensure maximum contrast and a minimum of glare from reflected light, and proper chalk, and may even place minimum limits on the size of letters and figures to be written on the blackboards.

Such a program may be expanded or contracted from year to year, reflecting any new advances in the fields of education, psychology, ophthalmology, architecture and engineering, and would survive curtailment of the school budget. It would even permit, occasionally, trial of newer technics of unproved value, without being seriously or permanently affected.

The consciousness of the value of good vision, which is the cornerstone of the program, must be laid in teacher-training institutions. All elementary-grade and intermediate-grade teachers should have some knowledge of visual psychology, as well as of ophthalmologic anatomy, physiology and hygiene. They should be instructed in objective and subjective signs of eyestrain, and should be so well versed in a dependable vision-testing technic that their findings will be accurate. Because the teacher has the unique opportunity of observing the child at work every hour of the school day throughout the school year, any eye-hygiene program that does not include the teacher will fall far short of its goal. There is a mutual benefit to be derived. A child who sees well and comfortably is less of a drain on the teacher's time and patience than the child with poor vision.

Historically, it is true that teachers, rather than physicians, were responsible for the enactment of legislation in Massachusetts that, since 1906, has required that every child in the public schools have a vision and hearing test at the beginning of each school year, and that the class teacher conduct the tests. The prescribed vision test is one designed to measure the acuteness of distant vision, and nothing more. Admitting that it would be better to know more than is now known about the visual efficiency of school children, I am certain that it is wrong for any individual or group to challenge the value of the results of the Snellen test, provided that it is properly conducted. This test is simple and reliable, and involves no expense; it takes a minimum of school time; it requires no special equipment, eliminating such factors as cost, transportation, breakage and replacement; and it brings about the discovery of about 85 per cent of children with visual and other eye defects. It might, indeed, discover 10 per cent more, if it were supplemented by a simple test for detecting farsighted children, who have normal distant vision but find near work difficult. For these reasons, the value of such a test should be defended against attacks by groups, many of whom have equipment to sell and who, in order to impress school authorities with the superiority of their devices for discovering rare and usually unsymptomatic conditions, such as extraocular muscle imbalance, suppression or alternate fixation, poor stereopsis and astigmatism, feel obliged to declare the Snellen test worthless and the school system that uses it archaic.

The test is absolutely dependable, but educational authorities seem to have little regard for the valuable information it furnishes, and consequently bother little about the manner in which it is conducted. The following examples of the

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misuse of the Snellen test in the public schools of Massachusetts since 1906 are illuminating:

> Teachers, having to rely on an instruction sheet that is furnished with the chart to guide them, often failed to observe one or more fundamental requirements, such as making sure that the eye not being tested was covered, or that the chart was placed where illumination would be adequate, and without glare from reflected light.
>
> Letter charts were used, which children committed to memory.
>
> The use of letters precluded the vision testing of kindergarten and first-grade and second-grade children, most of whom were, for the purposes of the test, illiterate.

The experience gained by school authorities during the first few years suggested the need of measuring the vision of younger children. They appealed to the State Department of Education, which in turn requested the Department of Public Health to recommend a test chart for illiterates. A subcommittee of the Council on Public Health, made up of Drs. David L. Edsall and William J. Gallivan, in 1915 recommended a chart (Fig. 1) for the use of teachers testing illiterates, which since 1917 has been distributed on request to the schools of the Commonwealth. This chart,

FIGURE 1.
The Boston Test Chart differs from other standard charts in that symbols on the 30 and 20 foot lines are spaced more than 5 minutes apart.

which is based on the Snellen scale, was partly devised by Snellen himself[1] as a test for illiterates, using three parallel lines. Pergens[2] later joined these lines on one side by a line of equal width. This is the most practical test object for use in schools, and moreover its use should not be limited to illiterates. It has three outstanding features. Firstly, after a short drill, conducted as a game, the vision of

FIGURE 2. *Old Method of Occlusion. This method, although dependable, required an extra teacher.*

children over two years of age may be accurately tested with it. Secondly, it is not to be compared with capital letters, which when made as uniform as possible are visible from different distances.[3] It therefore conforms more nearly than do other objects to the physiologic requirements for a test object. Finally, if the symbols are selected by the teacher conducting the test, as I[4] have recommended, even a small chart, such as that furnished by the State Department of Education becomes unlearnable.

A test chart that can accomplish so many things faithfully is no mean device. Competent ophthalmologists during the last quarter of a century have filled many pages of printed matter with a variety of unique test symbols, all carefully drawn to the Snellen scale, but none of these, so far as I know, compare with the Pergens symbol. As for some ludicrous and impractical technics suggested to prevent school children from memorizing test letters, the least said of them the better.

In a previous paper, I[4] suggested a technic for testing vision of school children. It required two

teachers to conduct it, because the occluder used was a card measuring 3 by 5 inches (Fig. 2), and if the children were allowed to hold it and the better

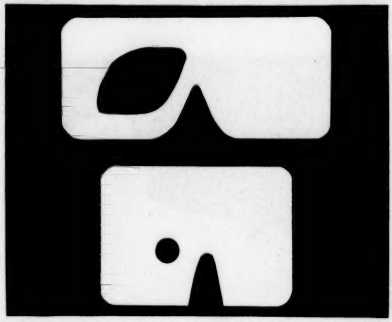

FIGURE 3. *Types of Occluders Used by the United States Navy. The newer form (above) permits observation of squinters and prevents artificial reduction of the size of the pupil by looking along the edge of the opening.*

eye was occluded, most of them peeked. The technic has been modified by substituting the more efficient occluder used by the Medical Department of the United States Navy (Fig. 3).

TECHNIC OF TESTING

The chart should be hung on an easel, blackboard or other device, near a window (but not in direct sunlight) and at right angles to it; it may be hung in the window casing. If one end of the room is brighter than the other, the chart should be placed at the brighter end. Its height should be about the level of the average child's head. If there is glare* from windows between the chart and the child, the lower half of the window may be covered or the shade drawn. This is rarely an obstacle unless the child, standing at the 20-foot line, is abreast of a window.

A distance of exactly 20 feet should be measured from the chart along the windowed wall, a thumbtack or chalk mark being placed on the floor or wall every 5 feet.

The occluder may be made of heavy cardboard, plastic or Masonite. The latter two materials are washable, even in antiseptics (a 1:1000 aqueous solution of Zephiran Chloride may be used). The occluder is held in the left hand with the opening in front of the right eye, which should always be tested first (Fig. 4). If the child wears glasses, he should be asked whether his vision is better with or without them. If it is better with glasses, the test should be made with them on, a notation to that effect being made on the record. If the vision is better without glasses, the test is made with them off.

*Glare is a brightness within the field of vision of such excessive character as to cause discomfort or interfere with vision.

The record will be more complete if the vision is tested both with and without glasses, in which case the vision of the naked eye is tested first. (If the vision is better without glasses, it should not be concluded that they are not correct; instead, reexamination should be advised, especially if the glasses are more than a year old.) After the right eye has been tested, the child holds the occluder in the right hand with the opening in front of the left eye, and that eye is tested.

When pointing to the symbols the examiner should not stand on the window side of the chart, lest a shadow be cast upon it (Fig. 5). The point of a pencil should not be used, since it may mark the card. The pointer must not cover any part of the symbol. A symbol on the top row is selected, and the child is told to semaphore the direction in which the arms of the symbol point. If his direction is correct, a symbol is selected on the second row. If the child's answer is correct, one on the third row is chosen. If the direction is correct, at least two symbols on the fourth row are selected, one with its arms pointing up or down, and the other with its arms pointing to the left or right. One must

FIGURE 4. *Method of Using the Occluder.*

glance at the child frequently to see that the occluder is kept in place, as well as to see that he semaphores correctly.

If the child reads two or more symbols on the fourth row, the vision is recorded as 20/20. If he

reads only to the third row, it is recorded as 20/30; if only to the second row, as 20/40; and if only the top row, as 20/50. He should be made to read at least two symbols on the lowest row that he can see in order to get credit for the row. If he cannot see the top row, he should be told to approach the chart — always with one eye covered — and stop where he can see two symbols on the top row. If, for example, he walks to within 5 feet of the chart, the vision is recorded as 5/50.

Follow-Up

Obviously, much of the time spent by school physicians and nurses in inspecting children's eyes and by teachers in testing their vision would be wasted if some provision were not made *by the school* to follow up cases of defective vision and other eye conditions discovered or suspected, soon after a notice has been sent to the parent or guardian. Expert medical advice is available in normal times to school children of all economic groups in the large cities; in small towns and in rural communities, this presents a problem. The optometrist may be the only person available to provide eye care of any sort, but this service, even though limited in scope, may suffice for a large percentage of children with refractive errors, especially myopes. The more complicated cases should be brought to the nearest ophthalmologist or eye clinic by the parent, the school nurse or some other designated person. The disposition of indigent cases should be the concern of the school principal or physician.

* * *

Figure 5. *Method of Using the Test Chart.*
The pointer should not mark the chart or cover any part of the symbol.

To recapitulate, the cornerstone of a workable, effective eye-hygiene program for school children rests on the development of a consciousness within the school system, especially among the teachers and pupils, of the value of normal vision to the progress of health and education. This may be developed through an educational program in the schools, sponsored by a joint committee of the State Department of Public Health and Department of Education. The committee's function should be to stimulate surveys by the school authorities in cities and towns throughout the Commonwealth. Interest might be created by first presenting to the heads of all school departments a copy of the statute requiring an annual vision test, together with an authoritative statement regarding the importance of conducting the tests properly, as well as obtaining relief for children early in the school year for those found defective.

With this accomplished, such a committee might arrange an outline for teachers, giving symptoms of eyestrain that may warrant a medical eye examination. Often a child with 20/20 vision in each eye suffers from sties, crusted red lids, watery eyes, irritated eyes or headache, especially after doing close work. Many of these children are farsighted, and if their accommodation is good, the Snellen test will not screen them out, but they suffer from and dislike close work, and are frequently truants. The committee might suggest a simple test for screening out this type of child at the time of the annual

vision test, even though this is not required by law.* Such children often require glasses for near work only, and may even leave them in school. It is of historical interest that Dr. Henry Willard Williams, first ophthalmic surgeon to the Boston City Hospital, presented a paper to the railroad surgeons of America in Chicago shortly after the Civil War in which he suggested this as a disqualifying test for railroad employees.

Such a committee could encourage the inclusion of some simple color-perception test, especially for junior-high-school pupils, who might be planning a career in art, aviation, the Navy or the textile industry. A few pieces of colored yarn or a half-dozen colored pencils would suffice to detect the color blind. The best approach to this group might be made through the Department of Vocational Guidance.

This work can progress to the study of regressive reading habits, heterophoria and stereopsis and to the gaining of other information that may be of importance in promoting normal educational progress. But before any of these are undertaken, the important thing is to find out whether every school child has normal vision. With this work well done we shall be better qualified to evaluate properly the new lighting fixtures, optical aids and ophthalmic correctional devices so highly publicized. In this way a goal may be reached that is worthy of the best American medical and educational tradition.

I am indebted to Lieutenant Commander E. H. Daniels, (MC), U.S.N.R., for calling the most recent type of Navy occluder to my attention.

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*The simplest test for this purpose is one of a battery of tests known as the Massachusetts test, developed by Oak and Sloane.[5] It is accomplished by placing a pair of spectacles containing plus spheres (+1.50 or +2.00) before the eyes of a child who has 20/20 vision. If he can still read 20/20, his farsightedness may well cause symptoms, either ocular or systemic, and reference for an eye examination is advisable.

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Correction. In the article "Pain and Disability of Shoulder and Arm Due to Herniation of the Nucleus Pulposus of Cervical Intervertebral Disks" by Drs. J. J. Michelsen and W. J. Mixter, which appeared in the August 24, 1944, issue of the *Journal*, the sublegend of Figure 2 should read as follows: "*The three types are as follows: 1 — herniation producing unilateral compression of the roots; 2 — herniation producing unilateral compression of the ventral cord (Stookey's Group II); and 3 — herniation producing bilateral compression of the ventral cord (Stookey's Group I).*"

MEDICAL PROGRESS

PHYSIOLOGY*

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THE last days of 1944 will bring a centenary as significant to physiologists and to all those whose concern is with experimental medicine as it is to surgeons and obstetricians. On the morning of December 11, 1844, Horace Wells, a dentist of Hartford, Connecticut, noticed the insensitivity to pain produced by nitrous oxide gas administered to Samuel Cooley by C. Q. Colton at a private exhibition, which followed a public lecture and a demonstration of "laughing gas" held the night before. Acutely conscious of the problem of pain in dental operations, because of the multiple extractions necessitated by an improved dental plate that he and W. G. Morton had devised somewhat earlier, Wells at once foresaw the practical application of the phenomenon he had witnessed. Enlisting Colton's aid, he returned to his office, where he inhaled the gas himself, while a fellow dentist removed a tooth that had been bothering him. Wells's subsequent efforts to introduce nitrous oxide as an anesthetic agent failed, and it was not until thirty years had passed that Colton, ever mindful of what he had seen in Hartford, persuaded another dentist to give public trial to the method, this time successfully. Wells's discovery nevertheless retains stature in the history of anesthesia, not only in the matter of priority as the second in the series of Long, Wells and Morton, but because of the intimate background this work forms to that of Morton, which introduced anesthesia to the world. Although in surgery equal honors are shared by asepsis and anesthesia, the former plays a lesser role in physiology, particularly in acute experiments and in species whose resistance to wound infection surpasses that of man. Anesthesia is, in truth, the cornerstone of physiologic technic, and the development of experimental medicine has been fostered in no insignificant way by the discovery that is shortly to be celebrated.

NITROGEN BALANCE IN STATES OF DAMAGE

In the progress report on physiology for 1941,[1] significance was seen in reports stressing the importance of high-protein diets in circumstances likely to be complicated by liver damage. Since then the subject of high-protein diets has attained a position as one of the most prominent factors in the care of patients suffering from infections, fractures or burns, and in fact from almost any condition that inflicts damage on the organism.

The protein requirement of everyday life has not lacked attention, and it is generally assumed that for the average adult a daily intake of 1 gm. of protein per kilogram of body weight[2] is adequate. This may be reduced to 0.5 to 0.7 gm. in the presence of a high intake of carbohydrate and fat,[3] owing to their protein-sparing activity. During pregnancy the protein intake may be increased by a half, and during lactation it should be two and a half times the usual amount.[2] Infants require no less than 4 gm. of protein per kilogram of body weight, and even at six years of age 2 to 3 gm. must be supplied.[4]

The increased protein requirements in typhoid fever have been recognized since 1909, and the work of Whipple demonstrated the importance of increased protein intake for the regeneration of hemoglobin during recovery from anemias. Peters and Bulger[3] called attention to the fallacy of restricting the intake of protein in the nephritic syndrome, and demonstrated that patients losing albumin through diseased kidneys were often seriously depleted of protein, and required as long as three months to restore their protein stores when placed on a more adequate diet.

The more recent developments in this field come from two sources: the recognition by surgeons of the importance of an adequate protein intake in promoting adequate wound healing and the discovery of important protein loss in the early days following trauma — the so-called "toxic protein loss." The first phase no doubt stems from the work of Clark[5] in 1919 on the influence of diet on the healing of wounds. He noticed that in dogs fed a fat-rich and protein-poor diet a period of quiescence occurred on suture of an experimental incision, which postponed by six days the beginning of healing and eventual recovery. Healing began at once in dogs fed a high-protein diet, shortening the time for full recovery by six days. Revived by Ravdin and his collaborators,[6] the work of Clark has been fully substantiated, and Koster and Kasman[7] have shown that the average concentration of plasma proteins in 40 cases of wound disruption was significantly lower than it was in 40 control cases of well-healed wounds. Difficulties due to a low intake of protein appear to be most serious in patients suffering from gastrointestinal disorders requiring surgery. This is partly because these patients have voluntarily

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restricted their diet owing to the symptoms of their disease, and Riggs, Reinhold, Boles and Shore[8] have recorded a somewhat lower average serum protein concentration in a group of ulcer patients (6.7 gm. per 100 cc.) than in a control group (7.2 gm. per 100 cc.). Since, as Taylor and others[4] point out, the serum protein level is maintained at the expense of body protein and a deficit of 1 gm. of serum protein indicates on the average a depletion of 30 gm. of tissue protein,[9] a moderate depletion of serum protein may indicate a substantial loss of protein from the body. In addition, surgeons have almost universally reduced the intake of patients undergoing surgery of the gastrointestinal tract. Intakes of 80 to 2200 calories a day are probably typical of this kind of treatment.[9] Far from helping either the patient or the surgeon, this procedure, or the depletion of protein resulting from it, causes edema of the gastrointestinal tract, which impedes the surgeon, slows emptying time and promotes vomiting, thus delaying recovery.[10–14] Since the total store of protein in an average adult body is around 2 kg., representing in the hydrated state as much as 11 kg., which if no other source of food were available would supply the basal caloric requirements of the body for only five days or thereabouts, it can be understood that starvation of a patient for five days to a week after operation may seriously deplete the available stores of body protein. A good part of these stores consists of muscle protein, which can hardly be considered as an inert material like fat. This depletion undoubtedly contributes largely to the asthenia seen in patients who have undergone major surgical intervention.

The second factor contributing to the deficit of protein in injury and illness appears to be a regular response to acute illness, whether it be the result of infection, trauma or burn. This toxic loss of nitrogen reaches a maximum on the fourth to the eighth day after the trauma,[15, 16] and may entail in a ten-day period the loss of as much as 137 gm. of nitrogen, over 850 gm. of dry protein or as much as 4 kg. of body substance. There is a concomitant rise in temperature and a parallel increase in basal oxygen consumption. In trauma, burns and hemorrhagic shock, there is an increase in blood sugar,[17] which according to some[18] may be an unrelated phenomenon, but in the view of others[19] it is certainly a part of the same mechanism. According to the latter, it represents the breakdown of tissue protein, either to supply glucose to meet the needs of the body for extra sugar in an emergency or to supply building blocks for repair in the damaged areas. However beneficial the immediate effects of an increase in blood sugar may be, its continuance can hardly fail to be harmful to the body. Whatever its function, its immediate stimulus may be the secretion of the gluconeogenic hormone of the adrenal cortex.[19]

To recapitulate, in a variety of medical and surgical conditions there may occur a considerable depletion of body protein owing to a combination of factors, of which the two most important are a generally diminished protein intake and an enhanced protein catabolism. This situation inhibits wound healing, renders the liver more liable to toxic damage, impedes the regeneration of hemoglobin, prevents the resumption of normal gastrointestinal activity and delays the full return of muscular strength. It is obvious that to meet the situation an adequate supply of proteins and calories must be made available to the body.

In many circumstances, an adequate intake cannot be maintained by mouth, and recourse must be had to parenteral administration. Plasma itself may be employed, since it is known from animal experimentation that an animal can be kept in nitrogen balance by the intravenous injection of dog plasma as the only source of protein.[20, 21] It is, however, metabolized in a somewhat different manner when injected than it is when taken by mouth,[22, 23] and there is some doubt that it is a complete protein.[24] The quantities that must be injected are too large to permit its use as a source of protein food.

Attention has recently been directed to the use of mixtures of amino acids produced by the pancreatic hydrolysis of casein as a ready source of the protein building blocks. Shohl, Butler, Blackfan and MacLachlan[25] were able to keep infants in positive and sufficient nitrogen balance when such casein digests, administered orally or parenterally, were the sole source of protein. Elman[24, 26] has given as much as 300 gm. daily for three days in a 5 per cent solution. He claims as advantages of the method that it rests the gastrointestinal tract without starving the patient, extends the limits within which surgery can be employed by improving the preoperative state, facilitates the surgical intervention itself by lessening edema in the gastrointestinal tract and minimizes postoperative complications. Others[16, 27] agree with these conclusions.

Others workers,[4, 10, 15] without renouncing the use of the intravenous route where it is necessary, have had recourse to the oral administration of high-protein diets, reinforced by fat and carbohydrate. If the patient is unable to take them naturally by mouth, they can be administered by intubation. When feasible, this method permits the administration of far more concentrated solutions, or even mixtures, than can be given by vein. When it is considered that Cuthbertson[15] found that diets containing as high as 230 gm. of protein and 4100 calories failed to eliminate the period of negative nitrogen balance, the obvious difficulties of giving protein by vein in a 3 to 5 per cent solution can be realized.[10, 28] This should not, however, become a matter for controversy; the simplest method should

be employed to assure that an optimum protein intake is maintained along with a high-calorie diet. This implies at least 150 gm. of protein and 3500 calories, with as much as 500 gm. of protein daily when trauma has been severe, as in serious burns.[4]

Dehydration

Accidents at sea have in the past directed attention to the requirements for an adequate supply of fresh drinking water, and dramatic incidents in the present war have brought the problem before the public in a spectacular manner. In professional and popular publications a variety of measures have been advocated to allay thirst at sea, including the juice that it is claimed can be expressed from fish, and enemas of sea water. A number of valuable research projects have arisen in response to this problem, and results are beginning to appear in unrestricted publications. One of these is a report by Futcher, Consolazio and Pace,[29] who made studies of water balance on 18 volunteers who spent the greater part of four days in pneumatic life rafts on the Gulf of Mexico in July. The weather conditions were such that the water requirement might be expected to approach the maximum to be found on any ocean. Average water loss by evaporation was calculated to be 730 cc. a day, and it was estimated that so long as exercise is kept to a minimum, clothing is kept moist with sea water and a light breeze blows, a supply of 500 to 1000 cc. of water a day will prevent the occurrence of dehydration in semifasting survivors on lifeboats and rafts in the tropics. Drinking water in these experiments was supplied by devices in which the salt in sea water is chemically precipitated.

Other experiments have covered the effects on the organism of varying degrees of dehydration. Earlier work by Coller and Maddock[30] indicated that serious signs of dehydration begin when about 6 per cent of the body's weight in water is lost. If this is lost without excessive sweating, sodium and chloride accumulate in the extracellular fluid of the body. In dogs deprived of water and food, loss of sodium and chloride is reduced practically to zero through the failure of the kidneys to excrete these substances.[31] The burro, an animal acclimatized to an environment of great heat, is said to sweat almost pure water, and even man guards against excessive loss of salt by reducing the amount of this substance in prolonged sweating.[31] The net result of this process is a growing hypertonicity of the extracellular fluids, including the plasma. Concentrations as high as 186 milliequiv. of sodium and 133 milliequiv. of chloride per liter of serum have been found in the dehydrated dog.[32]

Closely associated with the hypertonicity of the extracellular fluid of the body is an extra excretion of potassium — that is, one unassociated with nitrogen loss — in the urine.[33] This can only mean that potassium has moved out of the cell, along with cell water, and that this process mitigates the loss of extracellular fluid. Renal activity is essential for the process, for in animals with ligation of the ureters the phenomenon does not occur. Apparently, loss of potassium in excess of that derived from breakdown of tissue takes place in a number of circumstances in which the volume of extracellular fluid is reduced or the fluid in this compartment is hypertonic. Among the first to note the phenomenon were Gamble, Ross and Tisdall,[34] who detected it in fasting diabetic children, and concluded that it indicates dehydration of intracellular fluid as well as extracellular water loss. In diarrheal disease in children, Butler, McKhann and Gamble[35] noted that intracellular water was lost in quantities greater than was extracellular water. Atchley, Loeb and their co-workers[36] noted an increased potassium excretion during glycosuria or acidosis in diabetics, indicating that intracellular fluid participates in the dehydration developing in this condition. Excess potassium loss occurred even when sodium chloride was added to the dietary of salt-deficient animals,[37] and when dogs were bled to an extent of 2.0 to 3.5 per cent of their body weight.[38] These authors commented:

> We are accustomed to regard interstitial fluid as an extensive reservoir from which plasma losses can be readily replaced, its electrolyte composition being so nearly identical with that of the plasma. That water and the unsuitable electrolyte, potassium, should also be immediately withdrawn from tissue cells would not, on teleological grounds, be expected.

They found the potassium to have a concentration in the urine three times as great as that in cell water, indicating that cell water is retained in the plasma, whereas cell electrolytes, unsuitable for plasma construction, are excreted.

Ingestion or infusion of a variety of salts — sodium sulfate, ammonium chloride, urea and so forth — causes an extra excretion of potassium in the rabbit,[39] dog[40] and man.[41] Wiley and Wiley[42] followed the process somewhat more closely in a man.[42] They found that a normal man can be dehydrated to an extent of about 1.5 per cent of his body weight without any great disturbance of salt balance, presumably because of the ability of the organism to concentrate its fluids to some extent. With more marked dehydration — to 5 per cent of body weight — there was an initial loss of sodium and chloride and a persisting loss of potassium, which indicated that, although extracellular fluid is probably the first to respond to water deprivation, there is also a loss of cellular water. When further loss of water was avoided, there was a continued loss of body potassium and a retention of sodium, denoting that a shift from cells to blood serum and interstitial fluids was taking place. When, finally, water was administered in amounts sufficient to restore the original water content of the body, sodium was lost and potassium was retained. The authors concluded that most of this water was thus retained

in the cells and that most of the water lost during dehydration was lost from them.

The first inference that may be drawn is that the loss of potassium constitutes a mechanism whereby fluid losses may be spread over the whole of the body fluid, instead of being restricted to the somewhat smaller compartment that constitutes the extracellular fluid. Recent work indicates that another possible effect of potassium loss may be important, namely, that it provides a means for conserving sodium. With sodium loss it is known that the extracellular fluid is greatly reduced, as, for example, McCance[43] has shown in man following sweating, and that the general debility resulting therefrom is great.[44] Hopper, Elkinton and Winkler[45] have moreover offered evidence that the salt concentration of the extracellular fluid governs not only the total volume of extracellular fluid but also — and much more important — the partition between plasma and interstitial fluid. They call attention to the observation that severe chronic water depletion in the dog produces surprisingly little peripheral circulatory failure. This type of dehydration results in contraction of extracellular fluid volume without any considerable sacrifice of extracellular salt. On the other hand, dehydration of somewhat comparable severity, in which salt as well as water is lost, may regularly be followed by acute circulatory failure. These authors' conclusions are as follows:

> The view has been widely held that loss of sodium chloride is harmful mainly because it leads to a reduction in the volume of the extracellular fluid. This is based on the fact that, under many circumstances, loss of extracellular water does tend to parallel that of extracellular salt. It is assumed that this reduction of extracellular volume leads in turn to a proportional contraction of plasma volume, with consequent impairment of normal circulatory dynamics. Our experiments indicate that this simple conception can be only partially correct. Were the reduced volume of the extracellular fluid wholly responsible for the adverse effects on the circulation, the manner in which the reduction was effected would be immaterial. Such is not, however, the case. For example . . . the circulatory responses of Dog 12 to simple water deprivation and to loss of salt and water are compared. The decline in extracellular fluid volume was about the same with both procedures. Nevertheless, plasma volume was strikingly reduced and circulatory efficiency much impaired following salt withdrawal, effects which were absent with simple severe water loss. Here, obviously, changes in volume of extracellular fluid alone do not explain these differing circulatory reactions.
>
> Clinical experience supports the importance to the circulation of composition as well as of volume of the extracellular fluid. Parenteral administration of pure dilute glucose solutions to patients with shock associated with salt depletion tends to intensify rather than alleviate the circulatory impairment. This is true in spite of the fact that such glucose solutions do effect some expansion of extracellular volume. The expansion is, however, effected at the price of a further dilution of extracellular electrolyte.

The same workers sought also to study the cause of death in dogs deprived of food and water, by attempting to distinguish between the effects of fluid loss and hypertonicity per se. Dogs were made hypertonic without water loss by the intraperitoneal or intravenous injection of 5 per cent saline solution. Extracellular fluids became markedly hypertonic and intracellular fluid moved out from the cells, with the net result that the hypertonicity of the extracellular fluid was somewhat reduced, the volume of extracellular fluid greatly expanded and the intracellular fluid reduced in volume and hypertonic. Circulation remained good until death, and only inconsistent and inconsiderable electrocardiographic changes occurred. Death occurred because of respiratory paralysis, and the circulation failed only after respiration had ceased to be effective. The authors[32] conclude that intracellular dehydration, perhaps within the cells of the respiratory center, was the likeliest cause of death. Application of these studies to man may prove possible; they conclude:

> A clinical state comparable to that of our animals might result from the consumption of sea water by man. Vomiting or diarrhea, if present, would of course have deleterious effects other than those studied here. If, however, any or all of the sea water were absorbed, our results are relevant. Assuming that the reactions of man are at least qualitatively similar to those of the dog, the sequence of events following the absorption of sea water may be outlined. At first, there would be an increase in the total water of the body, with a disproportionate increase in the extracellular fluid and a decrease in the intracellular fluid. Since the large extracellular fluid would favor an adequate renal flow, increased urinary excretion of water and salt would be expected. This would approximate in volume the amount of fluid absorbed, so that in the end dehydration would not be mitigated. The concentration of salt in the urine would presumably be less than observed in our experiments, since the human kidney cannot concentrate urine quite as well as can that of the dog, and would certainly be less than its concentration in the ingested sea water. The final result would be an increase in the extracellular fluid, an equivalent decrease in the intracellular fluid and an increase in the tonicity of all the body fluids. It is not known whether death from respiratory failure has ever occurred in human beings who have carried this process far enough, but it is reasonable to predict its eventual development.

These suggestions are in a measure borne out by Fay, Altmann and Kondi,[46] who administered sea-water enemas to 3 fasting volunteers deprived of all fluids for eighty hours, and compared them with 3 controls who were fasting and deprived of fluid but did not receive the sea-water enemas. From 800 to 1200 cc. of sea water was administered daily. The sea water was undoubtedly absorbed, as evidenced by the higher blood and urine chlorides. There was an average added urinary excretion amounting to 600 cc., and the sea-water group lost on the average 10 pounds, as against 6 pounds in the controls. There were no signs of greater extracellular dehydration in the sea-water group, as shown by the fact that hemoglobin concentration, red-cell counts, cell volume and serum protein levels were the same in both groups. It must be concluded that the additional 4 pounds lost in the sea-water group was largely intracellular fluid and that, as in the experimental animals, extracellular volume was maintained at the expense of the intracellular dehydration.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 30401

PRESENTATION OF CASE

A forty-five-year-old man, a funeral director, entered the hospital complaining of pain and swelling of the left knee.

Two years before admission the patient first noted minor pains in the left knee, which he attributed to arthritis. For six months prior to entry he noticed, while walking, that the left knee felt insecure. Five weeks prior to entry, while walking on the street, the knee suddenly gave way from under him. There was no pain, but swelling occurred for the first time. He consulted a physician, who made x-ray studies of the knee and told him that he had a "bone tumor." The leg was placed in a posterior mold from heel to groin. He remained entirely comfortable until admission to this hospital. There had been no chills or fever or any redness about the knee. He had had no pain in any other joint.

So far back as he could remember he had had multiple small nodules on the extensor surfaces of the arms and the anterolateral surfaces of the thigh and legs. These had not increased in size or number and had never been painful.

Physical examination showed a well-developed and well-nourished man in no acute discomfort. There were multiple firm, ovoid, freely movable, nontender, subcutaneous nodules on the dorsal surfaces of both forearms and of the left thigh. There was a tender swelling over the lower portion of the left femur. Most of the tenderness was over the medial parapatellar aspect of the condyle of the femur. Examination of the heart, lungs and abdomen was negative.

The blood pressure was 130 systolic, 82 diastolic. The temperature, pulse and respirations were normal.

The urine was normal. The blood showed a white-cell count of 10,300, with 76 per cent neutrophils, and a hemoglobin of 15.8 gm. per 100 cc.

A roentgenogram of the lower end of the left femur showed destruction of the normal bony structure with preservation of most of the cortex. The cortex was thin, and anteriorly and laterally appeared to be broken through, with an accompanying periosteal reaction (Fig. 1). The joint surfaces were intact. There was no soft-tissue mass visible around the bones. Films of the spine showed that the left intervertebral foramen between the second and third cervical vertebras was increased in size, and there were pressure defects involving the bodies of the second and third vertebras in this area. Stereoscopic views showed flattening of the pedicles of the third cervical vertebra and probable, but not definite, slight enlargement of the intervertebral foramen. Films of the skull, arms and forearms were normal. A chest roentgenogram showed scarring in both apices, with calcification and fibrosis. There was scalloping of the inferior margins of several of the ribs, particularly the seventh on the left, but no definite soft-tissue masses were seen.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. FULLER ALBRIGHT: The diagnosis depends on the x-ray films and is not too difficult, I believe. Let us look at the films.

DR. MILFORD SCHULZ: This is the film of the knee made some time before entry. Here are the films taken at the time of his visit to the hospital. Between these examinations he developed a little more periosteal reaction.

DR. ALBRIGHT: I may be "all wet," but if this is not neurofibromatosis I shall be greatly surprised. The patient had multiple subcutaneous nodules. He had evidence of multiple enlargement of the nerves, with definite enlargement of one cervical foramen. He had a lesion in a very characteristic location for a neurofibroma, namely, the lower end of the femur.

The bone lesion in neurofibromatosis is not strictly a bone lesion but is an encroachment of a tumor of the nerve on the bone. The lesion is apt to occur where nerves enter the bone. In the anteroposterior view it often looks like a cyst; and in the lateral view one can often see — but not in this case — that the cyst-like appearance is due to a lesion on the outside extending into the bone. The most frequent site of the bone lesions in neurofibromatosis is the lower end of the femur. I am so confident that this is a case of neurofibromatosis that I brought along a few slides of some other cases for comparison. I will not consider any other diagnosis.

Here is a case of neurofibromatosis showing brown spots on the skin and subcutaneous nodules. The brown spots are characteristic. They have smooth edges like the coast of California, which are distinctly different from those in the disease that I have recently been interested in, osteitis fibrosa disseminata or what is perhaps a better name "polyostotic fibrous dysplasia," where the brown skin lesions

*On leave of absence.

have outlines resembling the coast of Maine. Note the occurrence of the lesion at the lower end of the femur. In the lateral view you can see how the lesion is extending into the bone from without. Here is another case showing exactly the same thing.

So far as I am concerned, this man had a neurofibroma. I shall, however, cover myself a little bit.

CLINICAL DIAGNOSIS

Benign giant-cell tumor of femur.

DR. ALBRIGHT'S DIAGNOSIS

Neurofibroma of femur.

ANATOMICAL DIAGNOSIS

Neurofibroma of femur.

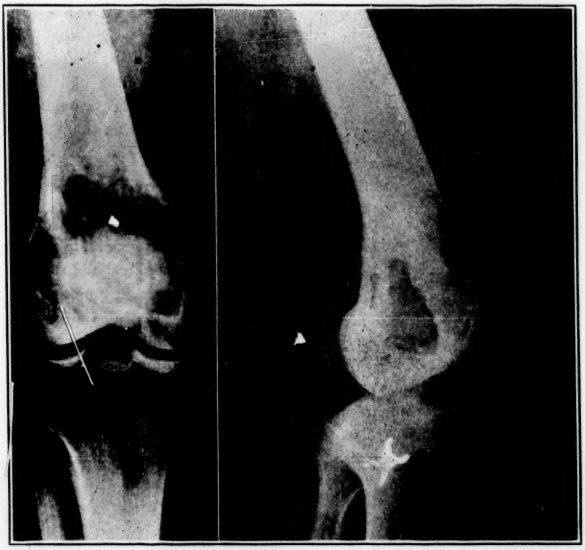

FIGURE 1. *Anteroposterior and Lateral Roentgenograms of the Femur.*

The question arises, Why was there a periosteal change in the x-ray films? I think that he had a fracture and that the periosteal proliferation was due to that. I have seen this same kind of periosteal reaction in an eosinophilic granuloma, but that is a poor second choice. And any other diagnosis I can think of is equally poor.

A PHYSICIAN: What about malignant disease?

DR. ALBRIGHT: Do neurofibromas ever become malignant?

DR. JOSEPH AUB: Yes.

DR. CHARLES S. KUBIK: Have we ever had a case with sarcomatous degeneration?

DR. BENJAMIN CASTLEMAN: Yes.

DR. KUBIK: Von Recklinghausen's disease, with other tumors?

DR. CASTLEMAN: Yes; I remember at least one, and I believe we have had others.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Because of the cystic character of the lesion, this patient was operated on with a preoperative diagnosis of benign giant-cell tumor. At operation the surgeon made a window in the very thin cortex, the surface of which was extremely rough, and a large amount of yellowish, friable and, in places, semi-liquid material poured out. The surgeon removed all this material with a curet, leaving a thin shell of bone around a cavity that included both condyles and extended up the femur for about 6 cm. I saw the material at the time of operation and thought that it looked grossly like a benign giant-cell tumor. I did a frozen section and could not see any giant cells, but I did see some foam cells, which are often present in a giant-cell tumor. When the final sections came through, it proved to

be a neurofibroma with areas of degeneration that contained a large number of foam cells (Fig. 2).

DR. LAURENCE L. ROBBINS: The lesions of neurofibroma of bone that we see usually have a characteristic appearance. They erode the periosteal margins of the bone, producing an indentation of the cortex. In this case, from the appearance of the x-ray, the lesion seems to have arisen within the bone, although it may have started in a periosteal nerve and, instead of extending outward, extended inward.

FIGURE 2. *Photomicrograph of the Tumor.*

ADDENDUM

DR. CASTLEMAN: The patient was well and free from symptoms for the following ten months, when he noticed enlargement of the knee. A roentgenogram (Fig. 3) showed an area of destruction just above the condyle that was not present in previous films. It also showed considerable periosteal proliferation extending up the shaft, with similar changes about the cavity filled with bone chips. A chest plate was normal. Since it was thought that the tumor had recurred and had become malignant, a mid-thigh amputation was performed.

The tumor involved the lowermost 10 cm. of the femur and had extended into the surrounding tissues, especially the popliteal and suprapatellar regions, to form large soft-tissue tumor masses. There was no involvement of the tibia, although the articular cartilage was eroded. Microscopically the change from the original tumor was striking. The cells were large and atypical, and mitoses were numerous (Fig. 4). This is an example, therefore, of a case of generalized neurofibromatosis in which one of the benign neurofibromas involving bone became sar-

FIGURE 3. *Anteroposterior and Lateral Roentgenograms of the Femur.*
Note the large, soft-tissue masses. The bone lesion is filled with bone chips. There is an area of destruction on the medial margin of the lower shaft and condyle.

comatous. We reviewed the slides of the original tumor, of which we had made a large number,

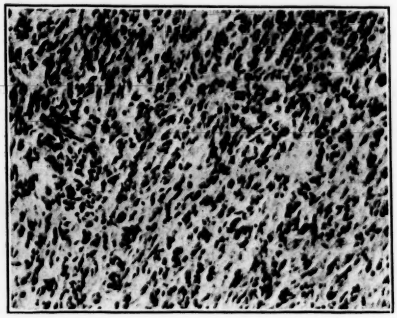

FIGURE 4. *Photomicrograph of the Recurrent Tumor.*

but could find not the slightest evidence of malignancy.

CASE 30402

PRESENTATION OF CASE

A six-week-old girl was admitted to the hospital because of "blue spells."

The infant was one of twins, delivered after an easy, normal labor, and weighed slightly over 4 pounds at birth. At the age of two weeks it was noted that she had difficulty getting her breath while feeding. This symptom persisted. Two days before entry she was taken to a pediatrician, who found an enlarged heart and liver. On the day of admission she had three episodes of cyanosis, the first being the severest and lasting forty minutes.

Physical examination showed a well-developed, fairly well-nourished, slightly dusky infant. The lungs were clear. The heart was markedly enlarged to the left, extending 2 cm. outside the midclavicular line and 3 cm. to the right of the sternum. No murmurs were heard. The sounds were distant. The liver was palpable 3 cm. below the right costal margin.

The temperature was 98°F., the pulse 120, and the respirations 60 to 80.

Examination of the blood showed a white-cell count of 10,640, with 46 per cent neutrophils, 8 per cent large and 44 per cent small lymphocytes and 20 per cent eosinophils.

X-ray examination of the chest showed a definitely enlarged heart without a characteristic configuration. An electrocardiogram revealed a sinus tachycardia, with a rate of 200, slight left-axis deviation, deep S_1, S_2 and S_3 and late inversion of T_1 and T_2; T_3 was upright. A repeat electrocardiogram seven days later showed no appreciable change.

The child was placed in an oxygen tent. The respirations fell to about 55 and she had no "cyanotic spells," but whenever she was out of the tent for half an hour to an hour the color became poor. Otherwise her condition remained unchanged until the eighth hospital day, when she started to cough and became cyanotic while being fed. She was put back into the oxygen tent but died five minutes later.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS: The electrocardiogram is obviously abnormal. It is more usual at this age to see right-axis deviation than left, although the latter may be present. Of course the T wave inversion in Leads 1 and 2 is abnormal. Other than that there is nothing about the pattern that gives any specific help. A heart rate of 200 does not suggest paroxysmal tachycardia in an infant. Sinus tachycardia as a direct result of heart disease is likelier.

In discussing the differential diagnosis there are three groups of congenital conditions — and I think it is obvious that this child had a congenital condition — that should be considered. The first group includes the mechanical defects of the great vessels, such as transposition of the trunks, defects of the valves, for example, aortic stenosis and pulmonary stenosis, and septal defects — auricular and ventricular. In order to make such a diagnosis one must have more evidence than I have here. No characteristic murmurs were heard. In a great many congenital defects an electrocardiogram is helpful in that high voltage and right-axis deviation are present, this being particularly true in infants who are deeply cyanotic. In this case, however, the electrocardiogram gives no assistance. One thing that helps a little in narrowing the field down is the degree of cyanosis. The fact that it was moderate and not constant rules out the congenital malformations characterized by marked cyanosis, transposition of the great trunks with septal defect, cor biloculare with persistent truncus and so forth. Those conditions are usually compatible with life for only a few days or weeks.

Another condition that must be considered is the tetralogy of Fallot, which usually is accompanied by more cyanosis than was noted here. Cyanosis, however, is not always present before the age of two. I believe that that diagnosis can be ruled out by the absence of characteristic murmurs and of evidence of right-axis deviation in the electrocardiogram. More frequent defects, such as an auricular septal defect, ventricular septal defect and patent ductus arteriosus, do not usually produce death at this age unless they are extremely large, and two of these conditions are associated with

characteristic murmurs, which this patient did not have.

One anomaly falling into this group that is consistent with the findings is abnormal origin of a coronary artery. Cases have been reported in which one of the coronary arteries, usually the left, rises from the pulmonary artery. In other cases there is only one coronary artery, which arises from the aorta. Ten years ago Dr. Paul D. White reported a case of an anomalous coronary in a boy three and a half months old who died following a series of attacks of cyanosis, sweating and dyspnea.* The child's electrocardiogram was grossly abnormal, with the most important changes in Leads 1 and 2, as they were here. The findings of cardiac enlargement without murmurs and a rather characteristic electrocardiogram are entirely in keeping with that diagnosis.

The second group of congenital disorders is that characterized by changes in the heart muscle itself. The most frequent is congenital idiopathic hypertrophy. Obviously the name is unsatisfactory. The group so designated is getting smaller all the time as more specific causes for hypertrophy are found. Many cases remain, however, in which the only finding at death is that of a large heart uncomplicated by any other anatomical finding. The findings in this case — the early death, the paroxysms of cyanosis and so forth — are entirely in keeping with this diagnosis. In the same group one must also consider von Gierke's or glycogen-storage disease, in which there is a disorder of glycogen metabolism. The most characteristic finding is that of hepatic enlargement. The heart may or may not be enlarged, but in some cases the heart enlarges proportionately more than the liver. Usually this is a chronic disease and patients live for years, but early deaths have been reported. I was interested in the description of the liver, which was said to have been definitely enlarged. That may mean something. The spleen was not enlarged. The absence of splenomegaly is another characteristic of glycogen-storage disease.

The third group to be considered is that characterized by lesions in the circulatory system outside the heart, especially in the lungs. A number of cases have been reported in these conferences — one of which I misdiagnosed — in which the chief lesion was a developmental defect of the pulmonary circulation. It usually consists of a lack of differentiation of the small radicles and capillaries into their usual subgroups which results, ordinarily, in a primitive, narrow circulation that obstructs the pulmonary flow. Such cases have been reported with findings similar to these. The only thing lacking in this case is an electrocardiographic pattern showing evidence of right-axis deviation.

*Bland, E. F., White, P. D., and Garland, J. Congenital anomalies of coronary arteries: report of unusual case associated with cardiac hypertrophy. *Am. Heart J.* 8:787-801, 1933.

In reaching a final diagnosis, there is one differential point of the greatest importance that cannot be answered with certainty. Was the enlarged liver the result of heart failure or of intrinsic liver disease (glycogen-storage disease)? A definite statement about the neck vessels might have answered that question, because when the liver enlarges as a result of heart failure, the neck veins almost invariably either are distended or show characteristic pulsation. Not having that statement I am forced to make a differential diagnosis that includes the three conditions, and I shall name them in the order of probability: idiopathic cardiac hypertrophy, glycogen-storage disease and an anomalous coronary artery. I cannot make a diagnosis of septal defect, valvular defect or an anomaly of the great vessels.

DR. T. DUCKETT JONES: I should like to ask Dr. Williams whether he thinks that, in general, the findings in the neck veins are as significant in children as they are in adults.

DR. WILLIAMS: Venous pulsation probably is. One does not often observe distended neck veins except in cases with a high degree of obstruction to the venous circuit. I do not see a great many infants, but my impression is that the neck veins show abnormal pulsations in the presence of increased venous pressure, even in infants.

DR. JONES: I have been impressed with the facts that in right-sided failure in young children the liver is easily palpable, and that neck signs, which might lead to an early diagnosis, are usually absent.

CLINICAL DIAGNOSIS

Congenital heart disease (idiopathic hypertrophy).

DR. WILLIAMS'S DIAGNOSIS

Congenital idiopathic cardiac hypertrophy?
Glycogen-storage (von Gierke's) disease?
Anomalous coronary artery?

ANATOMICAL DIAGNOSES

Glycogen-storage (von Gierke's) disease of heart.
Cardiac hypertrophy.
Coarctation of aorta, slight.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr. White saw this patient in consultation; he thought that the changes were consistent with a congenital anomaly of the coronary arteries and referred to the patient whom he had seen before.

The autopsy showed an enlarged heart, weighing 50 gm., which is about two and a half times the normal weight for a child of this age. The enlargement was uniform throughout the chambers, but slightly more prominent on the left than on the

right. The valves were normal. There was a slightly patent foramen ovale, which was probably of no significance. The aorta, just beyond the arch and at the level of the ductus arteriosus, which admitted a 2-mm. probe, was slightly narrow, so that I think that we can make a diagnosis of slight coarctation of the aorta. The liver was normal in size for a child of this age, weighing 125 gm., and all the other organs were normal.

Microscopic examination of the heart muscle proved that this was a case of glycogen-storage (von Gierke's) disease. The myocardial fibers were filled with glycogen, and even after fixation in formalin, in which ordinarily the granules are dissolved out, we were able to find the deposits of glycogen. There were relatively few granules in the liver. This falls in with the type of disease that is confined almost wholly to the heart, without involvement of the liver or kidneys.

DR. WILLIAMS: Was a urine examination reported? It is not given in the abstract, and it might have been helpful in the diagnosis if it had shown persistent acetonuria.

DR. CASTLEMAN: No examination is recorded.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

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Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

THE BLUE TRIANGLE

It will be readily appreciated that there will always be a large number of people who, for one reason or another, have not covered their catastrophic medical costs by prepayment insurance placed with commercial companies or with the Blue Shield or the Blue Cross, or both.

For about two years committees of the Massachusetts Medical Society and of the Massachusetts Bankers Association have been jointly considering a dignified postpayment plan for medical costs. The Association has gone into this plan extremely thoroughly, consulting proper authorities regarding the strategies, the legal aspects and the technical machinery of putting such a plan into effect. The Massachusetts Medical Society authorized its committee to participate in the planning and to initiate the program after the plans had been completed.

The groundwork has been accomplished. The plan — the Blue Triangle — is ready and will soon be put into operation. All members of the Massachusetts Medical Society will receive detailed information through their local banks. Each member should become thoroughly familiar with the opportunities provided by the plan and should make them known to those of his patients who might benefit thereby.

ANTIRETICULAR CYTOTOXIC SERUM

Considerable though brief interest was manifested in this country recently in a serum developed in Soviet Russia that was reported to have remarkable curative and healing properties. Some of the details concerning this remarkable discovery were presented at a special conference of clinicians and biologists that took place in Ufa in July, 1942. A brief report of the experimental and theoretical background and of some of the clinical applications of this serum is given in a series of papers published in the December, 1943, issue of the *American Review of Soviet Medicine*.

Over a number of years a group of Russian investigators, under the leadership of Professor A. A. Bogomolets, have conducted an extensive series of investigations on the effects of cytotoxic serums. Their results have led them to believe that small doses of antireticular cytotoxic serum stimulate mesenchymal cells, whereas larger doses block these cells. To prepare organotoxic immunizing serums for any animal, they use desiccated cells from another type of animal. Using cells of the spleen and marrow, they obtain serum that is cytotoxic to mesenchymal cells and that Doctor Bogomolets calls "antireticular." For use in human beings, the antireticular cytotoxic serum is prepared by immunizing animals with an antigen derived from the spleen and marrow of human cadavers. These organs must be obtained not later than six to ten hours after death in cases in which there has been no evidence of infectious disease.

On the basis of these studies and the reports of a number of clinicians, the Russian workers urged the use of this antireticular cytotoxic serum for the treatment of a wide variety of conditions, which include all types of infectious disease, particular mention being made of typhus fever, puerperal and gynecologic sepsis, rheumatic fever, tonsillitis, unresolved pneumonia, lung abscess and infectious diseases of the nervous system. They also believed that their clinical observations had established the therapeutic efficacy of this serum in war injuries of various sorts, including fractures, frostbites, second-degree and third-degree burns, early and late purulent infections of the cavities and tissues, and infected lesions of the eye. It was particularly effective in slowly healing infected wounds. They even felt justified in recommending its use in the treatment of neuritis, meningoencephalitis, disseminated sclerosis, senile and presenile psychoses, and schizophrenia. Some "encouraging results" were also obtained in the treatment of peptic ulcer, eczema and other "trophic" disturbances. Although not included in the list of indications, it is apparent that at least the senior author also thought that this substance might give favorable results in the prevention and treatment of cancer and senility. In fact, it was this author's interest in the latter that was largely responsible for the studies that led to the development of the serum.

These results may seem rather fantastic to "hard-boiled" American scientists who are accustomed to have extensive and thoroughly documented evidence presented for any new discovery of such far-reaching significance before they consider it even plausible. Before taking it seriously, they would undoubtedly like to see this work repeated by many independent workers under carefully controlled conditions. Unfortunately, the details of the Russian observations are not readily accessible in a form in which they can be properly evaluated by workers in this country. Until they are, one must consider these findings with an open mind.

At the time of the publication of these reports, the editor of the *American Review of Soviet Medicine* was apparently quite enthusiastic about the possibilities offered by this serum. Indeed, he was moved to write a note in preface to the issue, which ended in an appeal to expedite further studies with this serum. Clinical investigators in this country, who are not always easy to convince and who are usually quite wary of accepting such cure-alls, will undoubtedly prefer to await more detailed evidence of the efficacy of this agent before embarking on any clinical trials of their own. If one may judge from the tone of an editorial note printed in the following issue of the *American Review of Soviet Medicine*, it is evident that the former note was not enthusiastically received.

MASSACHUSETTS MEDICAL SOCIETY

EXECUTIVE COMMITTEE OF THE COUNCIL

On August 30, 1944, the Executive Committee of the Council, on the recommendation of the Committee on Membership and representatives from the supervising censors, took the following actions:

Allowed the following named fellows, applying for retirement and with all dues paid and in good standing, to retire under the provisions of Chapter I, Section 5, of the by-laws, such retirement to be effective as of January 1, 1944:

Cavanaugh, Thomas E. (Hampden), 293 Bridge Street, Springfield.
Dexter, Fred F. (Hampden), 151 Maple Street, Springfield.
Gorham, George H. (Norfolk), 91 Crest Avenue, Chelsea.
Johnson, Erik St. J. (Middlesex South), 8 Follen Street, Cambridge.
Ruble, Wells A. (Nonresident), 1929 East Glenoaks Boulevard, Glendale, California.

Allowed the following named fellows, applying for retirement, to retire with remission of dues owed the Society under the provisions of Chapter I, Section 5, of the by-laws, such retirement to be effective as of January 1, 1944:

Avedisyan, A. D. (Middlesex South), 164 Huntington Avenue, Boston.
Barton, John A. (Worcester North), 61 Fox Street, Fitchburg.
Ford, J. Francis (Norfolk), 8 Walter Street, Roslindale.
Hunt, Daniel L. (Suffolk), Hotel Vendome, Boston.
Nightingale, James (Worcester), 14 Puritan Avenue, Worcester.
Sargent, Oscar F., L. (Nonresident), 45 North Main Street, Farmington, New Hampshire.
Stevens, Harry L. (Bristol South), 133 Kempton Street, New Bedford.

Reinstated the following named physician, under the provisions of Chapter I, Section 10, of the by-laws, who had been deprived of fellowship for the nonpayment of dues, provided his arrears in dues at the time he was dropped plus the dues for 1944 be paid to the treasurer of the Society:

Wainshel, P. W. (Essex South), 92 South Common Street, Lynn.

Remitted the dues owed the Society, plus those of the present year 1944, of the following named fellow, who is ill and incapacitated, under the provisions of Chapter I, Section 6, of the by-laws:

Bartlett, Bernice A. (Essex North), 11 Haseltine Street, Bradford.

Accepted the resignations of the following named fellows, all with dues paid and in good standing, under the provisions of the by-laws, Chapter I, Section 7, the date of resignation to be as of January 1, 1944:

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Plouffe, Bernard L. (Worcester), 11 Hill Street, Webster.
Smith, John Hall (Middlesex South), Middlesex University, Waltham.

Accepted the resignation and remitted the dues owed the Society of the following named fellow under the provisions of the by-laws, Chapter I, Section 6 and Section 7, the date of resignation to be as of January 1, 1944:

Haskell, Helen S. (Hampshire), 135 East 65th Street, New York 21, New York.

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Kansas City University of Physicians and Surgeons, 1933. Sponsor: Carrie I. Felch, 541 Commonwealth Avenue, Boston.

DUTRA, FRANK R., 25 Shattuck Street, Boston.
Northwestern University Medical School, 1942.

FERREBEE, JOSEPH W., Harvard Medical School, Boston.
Harvard Medical School, 1934.

GREENFIELD, HAROLD B., 14 Coral Avenue, Winthrop.
College of Physicians and Surgeons, Boston, 1937. Sponsor: Jacob J. Abrams, 562 Shirley Street, Winthrop.

ILLINGWORTH, MYLES H., Boston City Hospital, Boston.
Tufts College Medical School, 1943.

INGALLS, RAYMOND G., 5 Bay State Road, Boston.
Tufts College Medical School, 1920.

LANDRY, CHRISTOPHER L., Boston City Hospital, Boston.
Tufts College Medical School, 1943.

ROIFF, HARRY S., 159 Shurtleff Street, Chelsea.
St. Louis College of Physicians and Surgeons, 1923. Sponsor: William Paris, 139 Washington Avenue, Chelsea.

ROTHMANN, EVA, 334 Commonwealth Avenue, Boston.
University of Berlin, 1927. Sponsor: Oscar J. Raeder, 270 Commonwealth Avenue, Boston.

TRAUNSTEIN, MAURICE, JR., 41 Bayview Avenue, Winthrop.
University of Vermont College of Medicine, 1942.

Robert L. Goodale, *Secretary*
330 Dartmouth Street, Boston

WORCESTER NORTH DISTRICT

GROSSMAN, MYER J., 352 Crescent Street, Athol.
Middlesex University School of Medicine, 1933. Sponsor: Francis X. Dufault, 245 School Street, Athol.

SCHECHTMAN, HAROLD I., 64 Milk Street, Fitchburg.
Middlesex University School of Medicine, 1934. Sponsor: Joseph D. Quinlan, 44 Prichard Street, Fitchburg.

Edward A. Adams, *Secretary*
44 Oliver Street, Fitchburg

DEATHS

BERMAN — Saul Berman, M.D., of Chestnut Hill, Newton, died September 18. He was in his forty-ninth year.

Dr. Berman received his degree from Harvard Medical School in 1920. He was formerly resident physician at the Boston Lying-in Hospital and was the founder of the Fertility Clinic and Laboratory at the Beth Israel Hospital. He was a member of the Boston Obstetrical Society.

His widow and three sons survive.

GAGNON — Alphonse P. Gagnon, M.D., of Taunton, died August 2. He was in his fifty-third year.

Dr. Gagnon received his degree from Tufts College Medical School in 1921. He was a member of the American Medical Association and the New England Society of Obstetrics and Gynecology.

His widow, a son and a daughter survive.

SPARROW — Charles A. Sparrow, M.D., of Worcester, died September 20. He was in his sixty-first year.

Dr. Sparrow was born in Marion and graduated from Amherst College in 1906, receiving his degree from Harvard Medical School in 1909. He was appointed to the staff of Memorial Hospital in 1916 and in 1925 became head of the Pediatric Clinic there. He was an associate editor of the *Worcester Medical News*, a publication of the Worcester District Medical Society, as well as a past president of that society and a councilor of the Massachusetts Medical Society. He was a member of the American Academy of Pediatrics and of the New England Pediatric Society.

His widow, a son, a daughter and a sister survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1944

RÉSUMÉ

DISEASES	AUGUST 1944	AUGUST 1943	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	137	24	15
Chancroid	2	*	*
Chicken pox	192	123	120
Diphtheria	6	5	12
Dog bite	1056	1064	1068
Dysentery, bacillary	18	14	15
German measles	57	72	31
Gonorrhea	426	374	432
Granuloma inguinale	0	*	*
Lymphgranuloma venereum	0	*	*
Malaria	49	13	2
Measles	227	346	281
Meningitis, meningococcal	34	34	4
Meningitis, Pfeiffer-bacillus	3	1	†
Meningitis, pneumococcal	1	2	†
Meningitis, staphyloeocal	0	0	†
Meningitis, streptococcal	0	1	†
Meningitis, other forms	0	0	†
Meningitis, undetermined	2	11	†
Mumps	273	137	143
Pneumonia, lobar	71	76	91
Salmonella infections	24	22	13
Scarlet fever	197	248	125
Syphilis	393	418	367
Tuberculosis, pulmonary	253	252	289
Tuberculosis, other forms	14	23	25
Typhoid fever	5	3	10
Undulant fever	7	5	4
Whooping cough	261	286	508

*Made reportable in December, 1943.
†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

Comment

Interest in the communicable disease situation centers this month on anterior poliomyelitis, both because of the seasonal increase in cases and because of outbreaks in certain other states. At present, the number of cases in Massachusetts is far below that of epidemic years, although greatly in excess of the seven-year median.

Salmonella infections were at nearly double the seven-year median for August. These cases, however, were widely scattered about the state.

Geographical Distribution of Certain Diseases

Anterior poliomyelitis was reported from: Adams, 1; Agawam, 1; Athol, 1; Barre, 1; Belchertown, 1; Boston, 5; Cambridge, 1; Chelsea, 1; Chicopee, 4; Dalton, 5; Deerfield, 4; Fall River, 2; Gloucester, 1; Great Barrington, 1; Groveland, 1; Haverhill, 5; Holyoke, 5; Lenox, 1; Ludlow, 1; Mansfield, 1; Marblehead, 1; Mattapoisett, 1; Natick, 1; Northampton, 2; Northborough, 1; Palmer, 2; Pittsfield, 21; Quincy, 2; Reading, 1; Revere, 1; Richmond, 1; Rockport, 1; Sandwich, 1; Sharon, 1; Southbridge, 1; Springfield, 39; Stockbridge, 2; Waltham, 1; Watertown, 1; West Springfield, 5; Westfield, 1; Whitman, 2; Wilbraham, 1; Williamsburg, 1; Williamstown, 1; Winchester, 1; Worcester, 1; total, 137.

Diphtheria was reported from: Boston, 3; Lowell, 1; Medford, 1; New Bedford, 1; total, 6.

Dysentery, bacillary, was reported from: Boston, 2; Lawrence, 1; Malden, 1; Milton, 1; Salem, 4; Worcester, 1; Wrentham, 8; total, 18.

Encephalitis, infectious, was reported from: Braintree, 1; total, 1.

Malaria was reported from: Boston, 4; Cambridge, 1; Camp Edwards, 15; Cushing General Hospital, 23; Lawrence, 1; Merrimac, 1; Somerville, 1; Springfield, 1; Weymouth, 1; Woburn, 1; total, 49.

Meningitis, meningococcal, was reported from: Agawam, 1; Beverly, 2; Boston, 14; Bourne, 1; Brockton, 2; Chicopee, 1; Dartmouth, 1; Gardner, 1; Lynn, 2; Somerville, 1; Springfield, 1; Sutton, 1; Swampscott, 1; Watertown, 1; Westfield, 1; West Bridgewater, 1; West Springfield, 1; Worcester, 1; total, 34.

Meningitis, Pfeiffer-bacillus, was reported from: Boston, 1; Cheshire, 1; Hampden, 1; total, 3.

Meningitis, pneumococcal, was reported from: Agawam, 1; total, 1.

Meningitis, undetermined, was reported from: Boston, 1; Rehoboth, 1; total, 2.

Rocky Mountain spotted fever was reported from: Chatham, 1; total, 1.

Salmonella infections were reported from: Attleboro, 1; Beverly, 2; Boston, 3; Lawrence, 3; Lynn, 1; Manchester, 1; Marblehead, 1; Melrose, 2; Needham, 1; Newton, 2; North Andover, 3; Rehoboth, 1; Springfield, 1; Worcester, 2; total, 24.

Septic sore throat was reported from: Boston, 1; total, 1.

Trichinosis was reported from: New Bedford, 1; total, 1.

Typhoid fever was reported from: Boston, 3; Charlton, 1; Worcester, 1; total, 5.

Undulant fever was reported from: Beverly, 1; Conway, 1; Falmouth, 1; Grafton, 1; Medway, 1; Norfolk, 1; Rutland, 1; total, 7.

Weil's Disease was reported from: Medford, 1; total, 1.

CORRESPONDENCE

ALKALINIZATION DURING SULFONAMIDE THERAPY

To the Editor: I was both surprised and pleased to read the editorial "Alkalinization During Sulfonamide Therapy," which appeared in the September 14 issue of the *Journal*.

The author of this excellent editorial, I believe, is correct in pointing out that the key problem to be solved, before the use of potassium bicarbonate is given widespread acceptance, is not its rationale, for that is obvious, but rather the toxicity of potassium bicarbonate when given in the large doses necessary to achieve adequate urinary alkalinization (18 to 22 gm. on the first day and 12 to 15 gm. on succeeding days).

We have not seen any toxic effects either in the cases reported in our paper or since then, but it is true that our experience has been relatively small. From our review of the literature it seemed that potassium retention was only seen in really terminal uremia; the other situation under which potassium toxicity might be expected — untreated Addison's disease coexistent with congestive heart failure — is a metabolic paradox and rare enough to be considered a medical curiosity. It must be admitted, however, that this point of view is not shared by all; thus, Dr. Paul D. White in the 1944 edition of his book *Heart Disease* states, "Calcium (and potassium) salts in high dosage should not be administered to digitalized patients because of the hazard of serious toxic effects on the cardiac mechanism."

Although further demonstration of the harmlessness of potassium salts is desirable, I do not believe that the suggestion advanced by the author of the editorial to avoid possible toxicity is practicable. He suggests the use of smaller doses (5 to 10 gm. daily) of potassium bicarbonate; but, unfortunately, although this might eliminate the possibility of toxicity, it would probably also abolish the beneficial therapeutic effect. The reason for this is to be found in the solubility curves of sulfadiazine and acetyl-sulfadiazine, which only begin to rise rapidly as the alkalinity of the urine approaches pH 7.4. I am afraid that 5 to 10 gm. daily would not often serve to render the urine alkaline enough to achieve the desired effect.

Although we believe that our dosage schedule is not likely to cause toxicity, I should like to suggest that instead of using smaller dosages of potassium bicarbonate alone, those who fear potassium bicarbonate toxicity use a mixture of potassium bicarbonate and sodium bicarbonate. If 10 gm. of potassium bicarbonate and 4 gm. of sodium bicarbonate are given daily, one would be within the generally accepted limits of safe potassium dosage and would also be able to achieve satisfactory alkalinization without giving more sodium than is contained in the ordinary hospital salt-poor diet. This is, of course, only a makeshift at best and should be abandoned if the concept of the low toxicity of potassium salts becomes established.

William Quitman Wolfson, M.D.
Greenpoint Hospital
Brooklyn 6, New York

A COMMUNITY BLOOD BANK

To the Editor: The editorial in the August 17 issue of the *Journal* pertaining to "Red-Cell Residues" is most excellent, commendable and timely. In the concluding sentences of the last paragraph, it reads: "One might think of each community with a blood-donor service prepared to supply whole blood, plasma, albumin, specific globulin fractions and erythrocyte suspensions. The proper use of such a service would require the co-operation of the physicians within the community, but the therapeutic possibilities are manifold."

May I call to your attention the fact that the Worcester District Medical Society has already established the type of service that the editorial portrays as a pious hope for the future. The Worcester blood bank, officially named the Worcester District Community Center for Aiding Transfusions, Incorporated, is sponsored by the Worcester District Medical Society and began its service to this community on October 12, 1942. It has given whole blood, plasma, erythrocyte suspensions and erythrocyte packs to any physician or hospital for the asking. In addition, we are serving the Lovell General Hospital at Fort Devens.

The cost of preparing this material is one of the lowest in the country, volunteer workers numbering over two hundred and only four full-time paid workers helping to keep the costs down. The expense of this service is supported in part by the patients receiving the material and in part by the Community Chest of Worcester.

This program is actual proof that a community without governmental help can successfully offer inexpensive community service. Furthermore, it can be said with emphasis that no one in the Worcester District has suffered from the lack of whole blood or blood components since this blood bank began its operations.

We believe that it is worth while to call this matter to your attention so that physicians in other communities can study the possibilities of community service without governmental dole.

William Freeman, M.D., *Secretary*
57 Cedar Street
Worcester, Massachusetts

BOOK REVIEWS

Roentgenographic Technique: A manual for physicians, students and technicians. By Darmon A. Rhinehart, M.D. 8°, cloth, 471 pp., with 201 illustrations. Philadelphia: Lea and Febiger, 1943. $5.50.

A careful reading of this book indicates, in the opinion of the reviewer, that the technic proposed by this writer is the one that was in use a decade ago. It gives practically no information to the radiologist or technician in a large hospital for special work referable to the skull, such as encephalography and ventriculography, which are frequently employed.

Nervousness, Indigestion, and Pain. By Walter C. Alvarez, M.D. 8°, cloth, 488 pp. New York: Paul B. Hoeber, Incorporated, 1943. $5.00.

The author, primarily a gastroenterologist, has long been interested in the nervous manifestations of diseases, particularly the resulting dysfunctions in the gastrointestinal tract. The book is the result of his long experience and is a personal report on what he has seen and recorded. He is thus in a position to evaluate many puzzling problems regarding one of the most complicated types of illness facing the general practitioner.

The book is full of sound advice, particular emphasis being placed on the diagnosis of disease from a complete history and physical examination from extensive laboratory data. The problems of constitutional inadequacy, nervous breakdowns and the menopause as well as many other topics, are handled with great skill. In reading the book one feels as though the author and his patient were in the same room and one was actually attending as an observer. The reviewer knows of no other book that so distinctively gives this impression. No one can read this book without being a better physician, and in it will be found the answer to many problems that have long been a trying annoyance to many practitioners. The various subheadings of the chapters give the tone of the book: "We, physicians, are giving our patients the impression that we diagnose only from laboratory reports"; "It is hard to take a good history without revealing one's knowledge as to the diagnosis"; "It is good to be somewhat neurotic"; "Nothing could be found at operation"; "The qualities desirable in the physician"; "Dilemmas that result from lying"; "Abdominal hallucinations"; "The woman who revels in medical treatment"; "The schoolteacher who tries every summer to get a master's degree"; and "What is the patient to do?"

This book is highly recommended.

Lincoln–Douglas: The weather as destiny. By William F. Petersen, M.D. 8°, cloth, 211 pp., with 16 illustrations. Springfield, Illinois: Charles C Thomas, 1943. $3.00.

The author has long been interested in the effects of cosmic disturbances on disease. He has written a number of books on the weather and its relation to epidemics and even to individual disease. In this volume he contrasts the environments under which Lincoln and Douglas were raised and developed. Their backgrounds were essentially dissimilar, Douglas being raised in Vermont in a prosperous family, the mother being in excellent health, and the other born under depressed circumstances in a log cabin, his mother being ill and probably suffering from tuberculosis. The body build of the two men was also distinctly in contrast, Douglas was short, rotund, broadchested, with square shoulders, small hands and feet, and of a buoyant, energetic, bustling personality; Lincoln, on the other hand, was excessively tall, stoop-shouldered, gaunt and awkward, with a shrill, squeaking voice. With these data the author investigates the weather conditions during the life of the individuals and attempts to correlate the influence that these had on the career of the two men.

The theory seems strained to meet requirements, and the book is not entirely convincing. The volume, however, is of interest to the medical profession for it deals with a topic much in current discussion. How much stress should be put upon weather as an effective agent in individual destiny is, to most scientists, an unanswered problem. The author believes that it plays an important role, even an outstanding one.

NOTICES

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday, October 6 — War Neuroses and Their Treatment in the Army. Major Jackson Thomas, U.S.A.

Wednesday, October 11 — Headaches Due to Ocular Disorders. Dr. Joseph J. Skirball.

Friday, October 13 — Deep Burns and Prophylactic Penicillin. Dr. Oliver Cope.

Wednesday, October 18 — Problems in Rhinology. Dr. Daniel Miller.

Friday, October 20 — Precordial Electrocardiography. Dr. Conger Williams.

Wednesday, October 25 — Pyuria in Children. Dr. James Marvin Baty.

Friday, October 27 — The Diagnostic Significance of Changes in the Appearance of the Tongue. Dr. H. J. Jeghers.

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases.

On Saturday mornings clinics will be given by Dr. William Dameshek.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Because of the holiday on October 12, the next regular meeting of the New England Dermatological Society will be held in the Skin Out Patient Department of the Massachusetts General Hospital on Wednesday, October 18, at 2 p. m.

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The regular fall meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary on Wednesday, November 15.

METROPOLITAN STATE HOSPITAL

The tenth Postgraduate Seminar in Neurology and Psychiatry will begin Wednesday, October 11, at the Metropolitan State Hospital, 475 Trapelo Road, Waltham. The program consists of fifty-four lectures and demonstrations in anatomy, applied physiology, pathology and roentgenology of the nervous system, clinical neurology and psychiatry. The lectures will be held every Wednesday from October 11 through December 13 and from January 3 through April 25, from 6 to 10 p.m. The seminar is open to all graduate physicians. Those interested are requested to register October 11 at 5:30 p. m. at the Metropolitan State Hospital.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 12

SATURDAY, OCTOBER 14
*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, OCTOBER 16
*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, OCTOBER 17
*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, OCTOBER 18
*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

OCTOBER 6–27. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Notice elsewhere on this page.

OCTOBER 9–20. 1944 Graduate Fortnight of the New York Academy of Medicine. Page xvii, issue of July 27.

OCTOBER 10. New England Society of Anesthesiology. Page xvii, issue of September 7.

(*Notices continued on page xv*)